DISSERTATION

on

COMPARATIVE ANALYSIS OF APACHE-II SCORE AND SOFA SCORE AS PREDICTORS OF MORTALITY IN PATIENTS ADMITTED WITH SEPSIS AND MULTI ORGAN DYSFUNCTION SYNDROME

Submitted in Partial Fulfillment of Requirements for

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CERTIFICATE

This is to certify that the dissertation titled **"COMPARATIVE ANALYSIS OF APACHE-II SCORE AND SOFA SCORE AS PREDICTORS OF MORTALITY IN PATIENTS ADMITTED WITH SEPSIS - MULTI ORGAN DYSFUNCTION SYNDROME"** is a bonafide work done **by DR.E.SENTHIL KUMAR**, Post graduate student, Institute of Internal Medicine, Madras Medical College, Chennai -03, in partial fulfillment of the University Rules and Regulations for the award of Degree of MD General Medicine (Branch-I), Internal Medicine, under our guidance and supervision, during the academic year 2013 – 2016.

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DECLARATION

I solemnly declare that the dissertation titled "**COMPARATIVE ANALYSIS OF APACHE-II SCORE AND SOFA SCORE AS PREDICTORS OF MORTALITY IN PATIENTS ADMITTED WITH SEPSIS AND MULTI ORGAN DYSFUNCTION SYNDROME"** is done by me at Madras Medical College , Chennai – 600 003 during the period April 2015 to September 2015 under the guidance and supervision of **Prof**. **Dr. G. SUNDARAMURTHY** submitted to the Tamilnadu Dr.M.G.R Medical University towards the partial fulfillment of requirements for the award of M.D. DEGREE IN GENERAL MEDICINE (BRANCH-I) .

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Last but not the least, I wish to thank all the patients without whom the study would have been impossible.

ABBREVIATIONS

ACCP	american college of chest physicians
AKI	acute kidney injury
APACHE	acute physiology and chronic health evaluation
ARDS	adult respiratory distress syndrome
CRP	c reactive protein
DIC	disseminated intravascular coagulation
IL	interleukin
LPS	lipo polysaccharides
MAHA	micro angiopathic hemolytic anemia
MODS	multi organ dysfunction
NF KB	nuclear factor kappa B
PAMP	pathogen associated molecular patterns
SCCM	society of critical care medicine
SIS	surgical infection society
SOFA	serial organ failure assessment
TLR	toll like receptors
TNF	tumor necrosis factor alpha

CONTENTS

INTRODUCTION

INTRODUCTION

In a tropical country like India, infections contribute to a majority of morbidity and mortality. Sepsis and secondary multi organ failures continue to challenge the health system. There continues to be global demand to improve the medical care to tackle such conditions. Scoring systems have been formulated to assess the severity of critical illnesses including sepsis and they provide prognostic information to the treating physicians.

These severity scores help in stratifying the patients and facilitating the prediction of disease outcomes based on certain variables. With the aid of such evaluation system we orient the limited resources towards more suitable patients. These scoring systems have the following merits

- Objective evaluation of the patient
- Improved triage system
- Improved therapeutic decision making
- Easier medical administration
- Better Medical auditing
- Use in randomised controlled studies and research

One of the most widely used severity of illness score is the APACHE II score (Acute physiology age chronic health evaluation score). This score was first formulated by William Knaus and others at

George Washington University Medical Centre in 1981 and it has continued to remain as valuable tool in evaluating accurately the severity of critical illnesses. The SOFA score (Sequential organ failure assessment score), another prognostication score was introduced in 1994 and is based on the degree of organ dysfunction.

A study by Q Qiao et al comparing the APACHE 2and SOFA score in critically ill elderly patients showed that SOFA had a better predictive capacity of mortality than APACHE 2.

Another study by K.S.Abinandan et al also showed that serial SOFA was a better mortality indicator in cases of sepsis and MODS.

However studies by K.M. Ho, K.Y. Lee et al showed that APACHE II score was a better predictor of mortality than SOFA score

So in this observational study, I chose to assess the presenting APACHE II score and SOFA score of patients admitted with sepsis with multi organ dysfunction syndrome and compare them both as predictors of mortality.

AIMS

AND

OBJECTIVES

AIM AND OBJECTIVES

To determine and compare APACHE II score and SOFA score as predictors of mortality in patients admitted with sepsis and MODS.

REVIEW

OF

LITERATURE

REVIEW OF LITERATURE

SEPSIS

Sepsis is a clinical syndrome that occurs as a complication of a serious infection and it has a significant associated morbidity and mortality. The focus of infection induces a cytokine storm that produces a spectrum of systemic insults like generalised vasodilatation , increased capillary permeability and leucocyte infiltration , finally culminating in widespread tissue damage[1,2,3,4]. Severe sepsis can result in a condition termed “multi organ dysfunction syndrome (MODS)” which has a high mortality even in developed countries. Despite the significant medical advances in the recent times severe sepsis continues to remain a killer disease[5,6].

Sepsis is a condition with varied manifestations and is turning out to be a major challenge to the health care providers. An improved understanding of the etiology and pathogenesis of sepsis along with its early recognition and early institution of evidence based treatment strategies is a pressing need. The definitions, incidence, etiopathogenesis and outcomes are discussed in the following sections.

HISTORICAL ASPECTS

The word sepsis is assumed to be derived from the Greek word "sipsi" which means "to make rotten " [7,8]. There are ancient manuscripts like the Edwin Smith papyrus of Egypt which document the suppurative lesions, especially those that followed the traumatic wounds and their systemic manifestations[9,10].

Hippocrates assumed that sepsis is the process of rottening of flesh and festering of wounds and that it is the pathway leading to generation of foul air in swamps. Galen had a different point of view. He proposed that sepsis aids wound healing. At arond 1000 BC , Ibn Sina had noted that fever was related to " putrefaction of blood " [11,12,13,14].

In the early seventeenth century Hermann Boerhave proposed that sepsis was probably mediated by the toxic substances present in air. In the nineteenth century the understanding of sepsis improved when Semmelweis demonstrated the co-relation between contaminated hands and puerperal sepsis. He realised that a simple procedure like hand washing with chlorinated lime solution before a gynaecological examination would reduce the chances of puerperal sepsis[15,16,17]. Subsequently the study of sepsis was taken forward by the pioneering works of Louis Pasteur and Robert Koch[18,19,20]. An English surgeon ,

Joseph Lister made landmark studies regarding the anti septic management with carbolic acid [20,21]. The German physicians Lennhartz and Schotmuller proposed that sepsis spreads out into the blood stream from the primary site via the bacterial toxins rather than the bacteria per se [22,23].

In the late nineteen sixties , Asbough et al discovered that severe sepsis could result in florid inflammatory response , particularly in the respiratory system thereby producing the diffuse alveolar infiltrates of the Adult Respiratory Distress Syndrome (ARDS) [24,25]. Similar studies proved that sepsis occurs secondary to a dysregulated immune response and not merely due to the direct toxic effects of the invading microbes. With more path breaking discoveries of the various micro organisms and a better armamentarium of antibiotics, the management of sepsis has transformed significantly. In 1991 an international consensus conference was convened by the American College Of Chest Physicians (ACCP) and the Society Of Critical Care Medicine (SCCM) to define the spectrum of sepsis and allied conditions. This was subsequently revised in 2001[26,27].

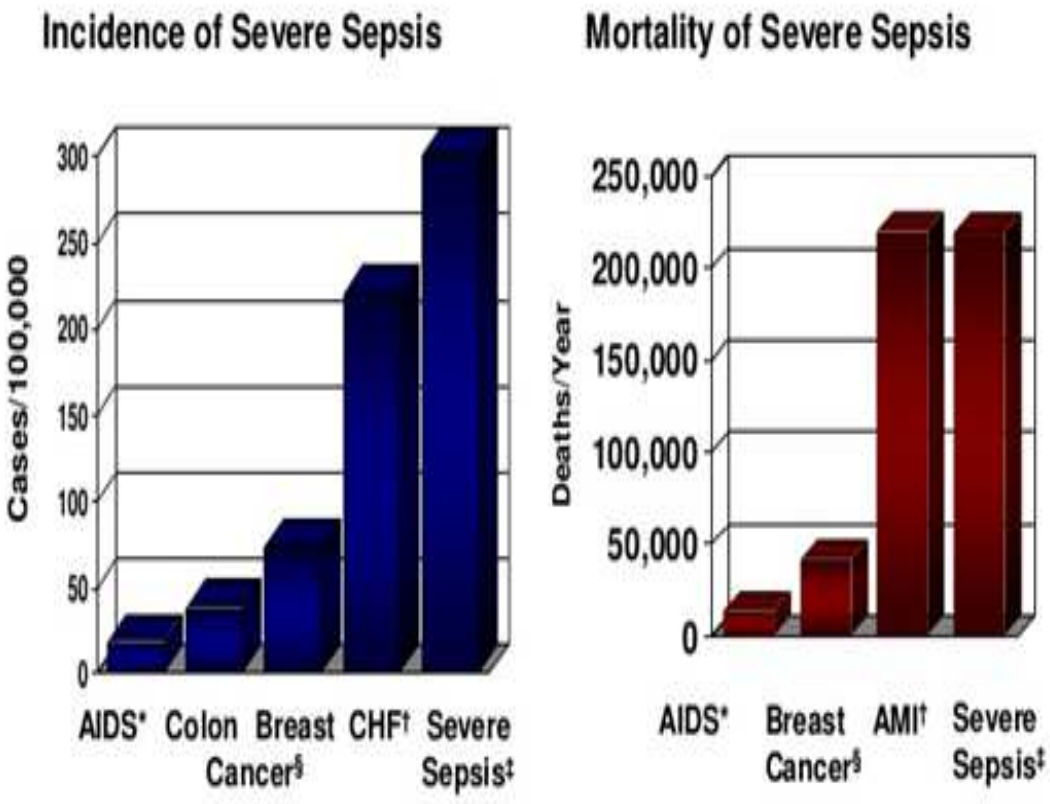
INCIDENCE

The annual global incidence and mortality of sepsis is estimated to be 13 million and 4 million respectively. The mortality rates of severe sepsis is as high as 50%. The global incidence of sepsis and its complications show a consistently rising trend on account of the

1. Aging population
2. Multiple comorbid conditions
3. increased immunosuppressive states
4. Expanding spectrum of micro organisms.

Sepsis, as a cause of mortality ranks much higher than the other major killer diseases as illustrated by the following picture[28,29]

INCIDENCE OF SEPSIS COMPARED WITH INCIDENCE OF OTHER MAJOR DISEASES



Angus DC et al Critical care medicine 2010

CHF - Congestive heart failure , AMI - Acute Myocardial Infarction

DEFINITIONS

Based on the consensus among international experts specific definitions of sepsis and allied conditions have been formulated.

SIRS or systemic inflammatory response syndrome may be defined as the presence of two or more of the following parameters

1) Temp < 36 or >38.3 degree Celsius
2) Heart rate > 90
3) Respiratory rate > 20
4) WBC count > 12, 000 or < 4,000 or band forms more than 10 %

Some experts advocate the inclusion of two more criteria namely acute onset of altered sensorium and increased plasma glucose[30,31,32] .

The term *infection* refers to the presence of micro organisms in an otherwise normally sterile body cavity or fluid (eg Urinary Tract) or the presence of an inflammatory response to microbes in body cavity or fluid that normally harbour micro organisms (eg GIT) [33,34].

Sepsis may be defined as the presence of two or more criteria of SIRS in the context of a documented or clinically suspected infection .

But the diagnostic criteria of sepsis was further modified in 2001 - international conference convened by the Society Of Critical Care Medicine (SCCM), European Society of Intensive Care Medicine (ESICM), American College Of Physicians (ACCP) , American Thoracic Society (ATS) and Surgical Infection Society (SIS). It includes the following parameters, as shown in the following table

General parameters

Fever (core temperature >38.3°C)

Hypothermia (core temperature <36°C)

Heart rate >90/min or >2 SD above the normal value for age

Tachypnoea: >20/min

Altered mental status

Significant oedema or positive fluid balance (>20 ml/kg over 24 h)

Hyperglycaemia (plasma glucose >120 mg/dl or 6.7 mmol/l) in the absence of diabetes

Inflammatory parameters

Leukocytosis (white blood cell count >12 000/μl)

Leukopenia (white blood cell count <4000/μl)

Normal white blood cell count with >10% immature forms

Plasma C reactive protein >2 SD above normal value

Plasma calcitonin >2 SD above the normal value

Haemodynamic parameters

Arterial hypotension (SBP <90 mmHg, MAP <65 mmHg, or a decrease in SBP >40 mmHg in adults or <2 SD below normal for age)

Mixed venous oxygen saturation <65%

Central venous oxygen saturation <70%

Cardiac index >3.5 l/min

Organ dysfunction parameters

Arterial hypoxaemia (PaO_2/FiO_2 <300)

Acute oliguria (urine output <0.5 ml/kg/h for ≥2 h)

Creatinine >176.8 mmol/l

Coagulation abnormalities (INR >1.5 or aPTT >60 s)

Ileus (absent bowel sounds)

Thrombocytopenia (platelet count <100 000/μl)

Hyperbilirubinemia (plasma total bilirubin >34.2 mmol/l)

Tissue perfusion parameters

Hyperlactataemia (>2 mmol/l)

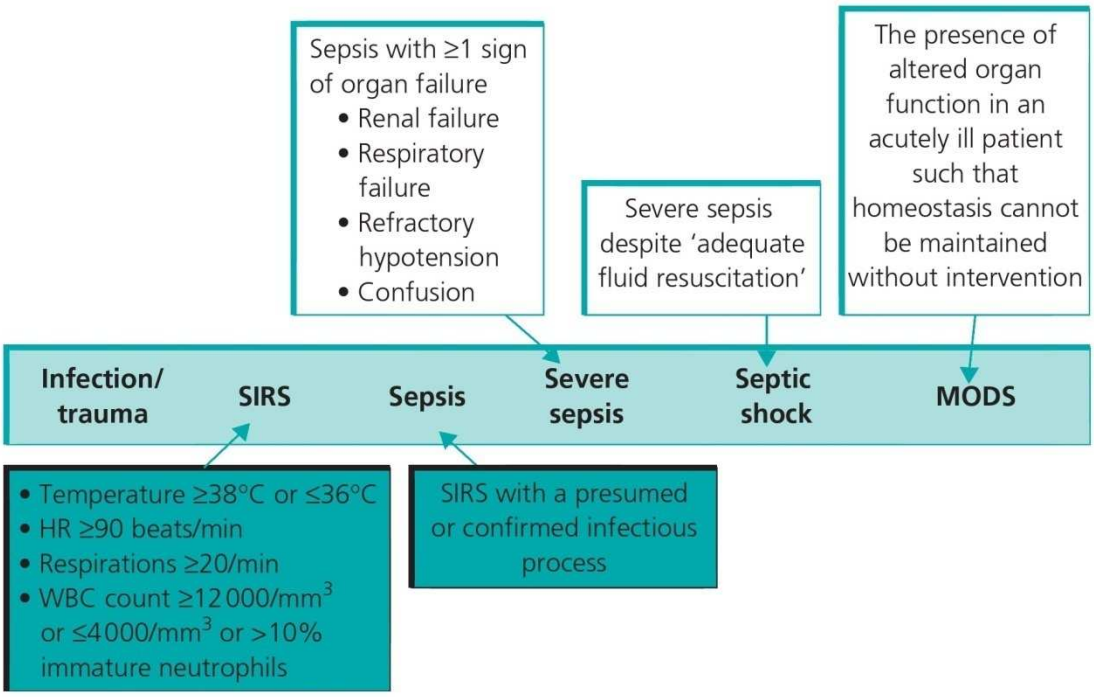
Decreased capillary refill or mottling

Septic shock may be defined as the presence of persistent hypotension in spite of adequate fluid resuscitation.

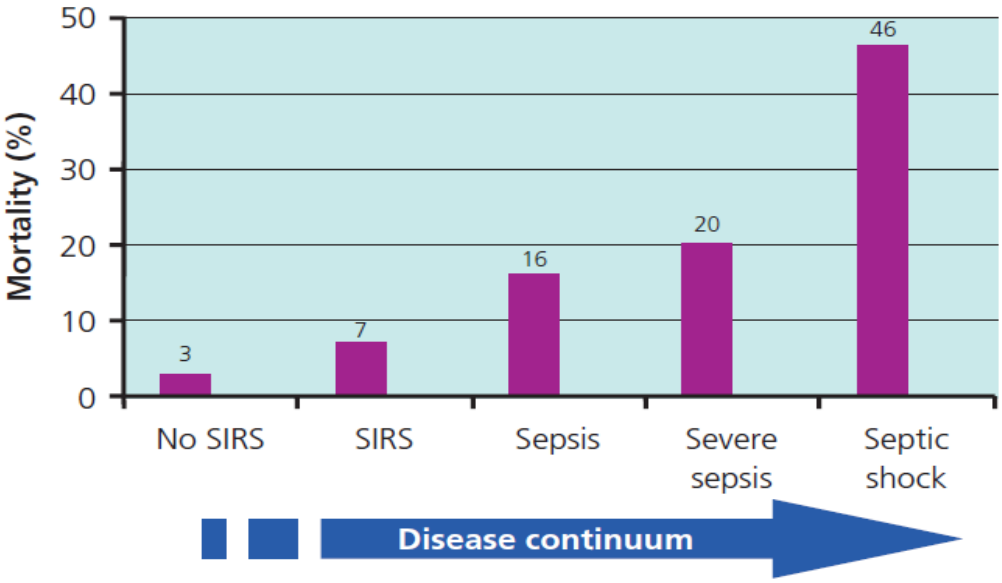
MODS or Multi Organ Dysfunction Syndrome may be defined as the clinical syndrome which is associated with progressive and potentially reversible dysfunction of two or more organ systems.

Thus these entities are a part of the continuous spectrum of sepsis.

THE SPECTRUM OF SEPSIS AND ASSOCIATED MORTALITY



SEPSIS – A DISEASE CONTINUUM

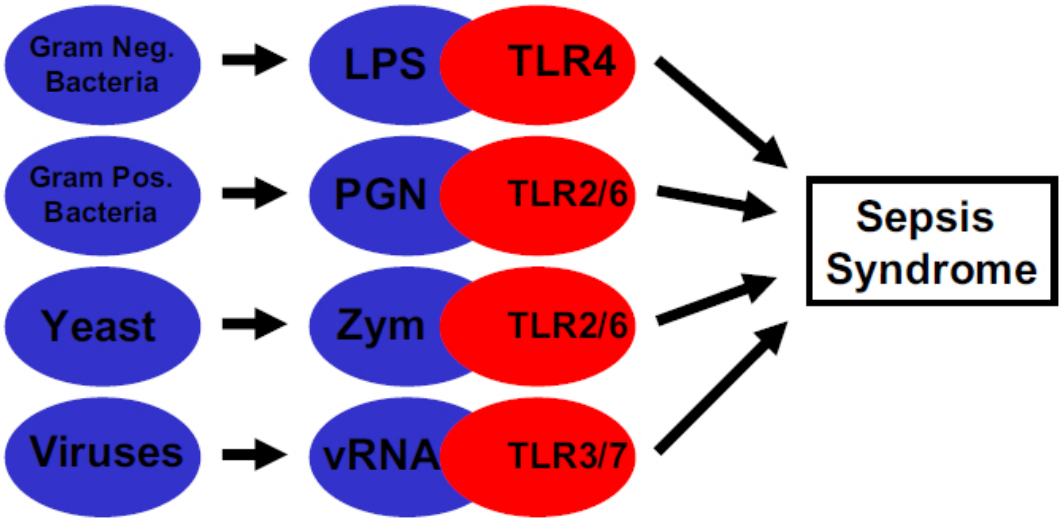


PATHOPHYSIOLOGY OF SEPSIS

Sepsis occurs as a result of the complex interplay between the infective organism and the host immune system. The innate immune system which forms the first tier of defence against the invading microbes is chiefly responsible for the unregulated inflammatory response that leads to sepsis. The innate immune system is comprised of the monocytes, macrophages, natural killer cells , endothelial cells and the dendritic cells[35,36,37]. When the micro organism enters the body , it stimulates this non specific innate immune response via the *Toll like*

receptors (TLR). These receptors are so called since they resemble the *toll receptors* found in Drosophila.

The TLR s attach to proteins called the Pathogen Associated Molecular Patterns (PAMP) which are highly conserved sequences present in the various micro organsisms. The PAMPs are usually comprised of lipo-polysaccharides or LPS (in Gram negative organisms) and petidoglycans (in Gram positive organsisms). The TLR then sends intra cellular signals to initiate the activation of transcription factors like the nuclear factor kappa b (NF KB). Subsequently there occurs production of inflammatory molecules like the interleukins (IL-1 , 6 , 8) , tumor necrosis factor alpha , cyclo oxygenases and prosta glandins. Then there is a secondary adaptive immune response mediated by the T lymphocytes and B lymphocytes. The interaction between the TLR and the PAMPs are depicted in the following picture

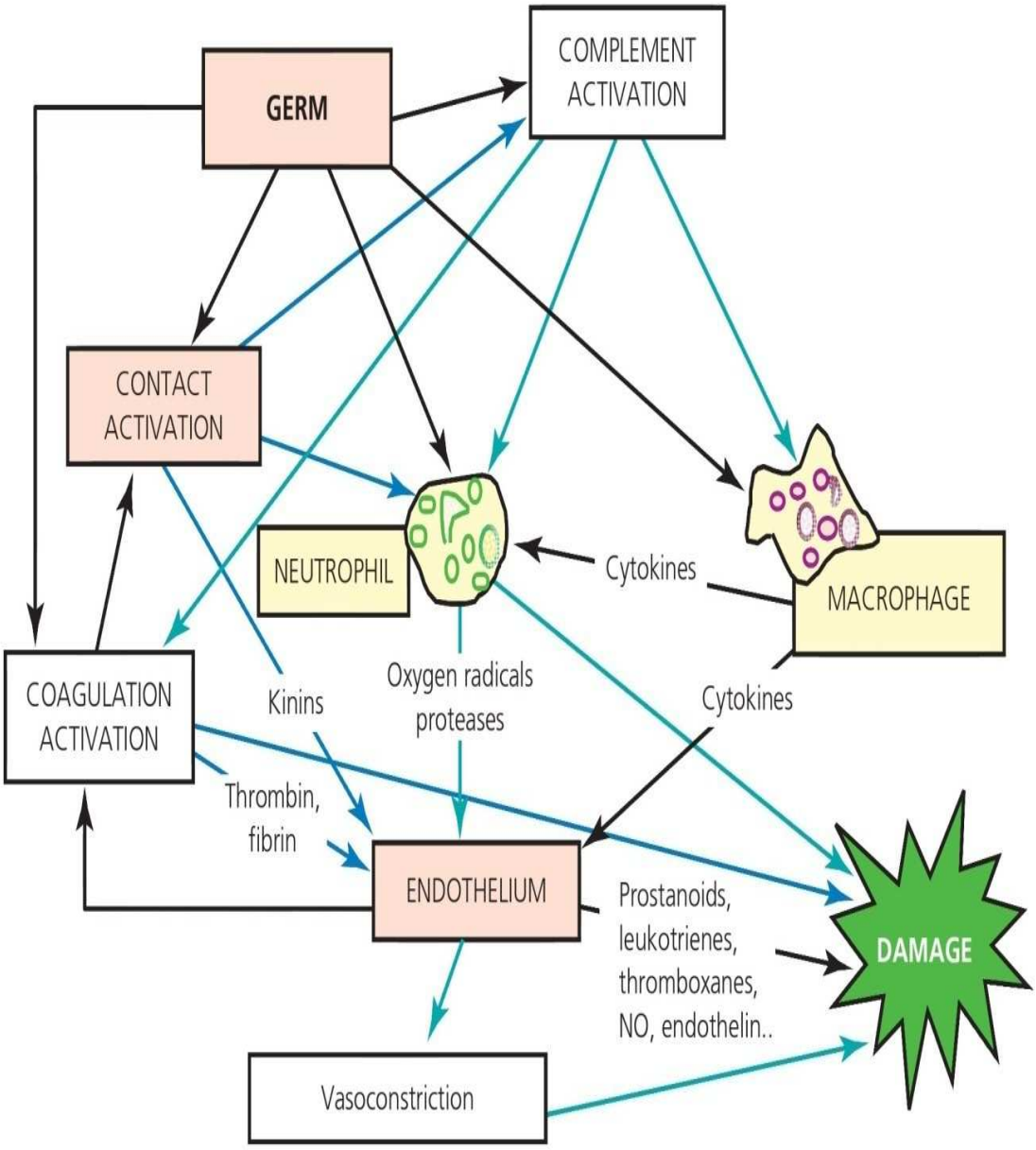


There are more than 10 TLRs each having an affinity for a different microbial antigen. Of these the most important is the TLR 4 which binds to the lipopolysaccharide component of Gram negative organisms and thus plays a vital role in the pathogenesis of Gram negative septicemia. It is also to be noted that even endogenous substances like heparin sulphate , hyaluronate , fibronectin , heat shock proteins , fibrinogen and certain polymeric sugars may also stimulate the TLR pathway. This explains the development of a systemic inflammatory response even in the absence of an infection in conditions like pancreatitis[38,39,40]. Some of the common TLRs and their specific ligands are illustrated in the subsequent figure.

TLR	Ligands
TLR1 (heterodimer with TLR2)	Triacylated lipopeptides, lipomannans from *Mycobacterium tuberculosis*
TLR2 (often dimer with TLR2 or 6)	Lipoproteins, peptidoglycans, lipoteichoic acids, yeast zymosan
TLR3	Double-stranded RNA
TLR4 (homodimer plus CD14 and MD2)	LPS, heat shock proteins, pneumolysin, respiratory syncytial virus coat proteins, heparan sulphate fragments, fibrinogen peptides
TLR5	Flagellin
TLR6 (heterodimer with TLR2)	Diacylated lipopeptides
TLR7	Responds to synthetic nucleosides and imidazoquinoline antivirals; native ligand is thought to be single-stranded RNA in endosomes
TLR8	Same as for TLR7
TLR9	Bacterial DNA—unmethylated CpG motifs
TLR10	Ligand unknown but TLR10 expressed in lung and B lymphocytes
TLR11	Uropathogenic bacteria in mice; absent in humans

The invading micro organsim interacts with innate immunity, adaptive immunity, the vascular endothelium and the coagulation pathways to bring about the septic response.

PATHOGENESIS OF SEPSIS



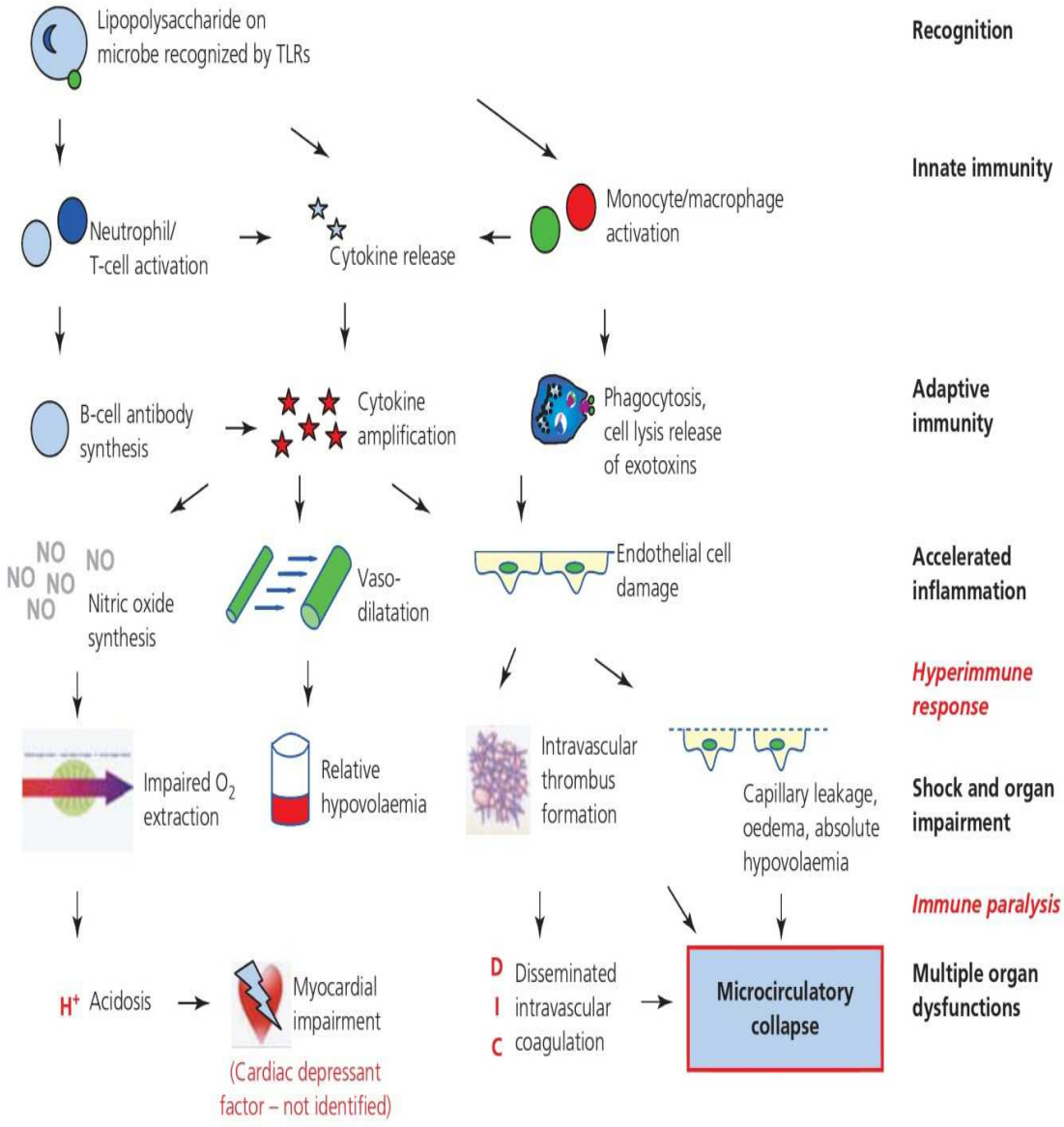
ROLE OF VASCULAR ENDOTHELIUM

The vascular endothelium has an important role in the pathogenesis of sepsis. The endothelial cells may be stimulated either directly by the bacteria or by means of the bacterial products. The response of the endothelium depends on the age of the patient , gender , co-morbid conditions , host genetic factors and on the characteristics of the invading micro organism. Impairment of the endothelial function results in morphological and functional changes which result in the following effects

- Uncontrolled release of vaso active substances like nitric oxide and prostacyclins
- Hyper reactivity of the vascular smooth muscles in response to vaso constrictive agents
- Adhesion and Migration of leucocytes
- Platelet activation and aggregation
- Imbalance between pro coagulants and anti coagulants
- Increased pro apoptotic substances
- Loss of barrier function

Thus the septic response is secondary to a complex interaction between the components of the microbe (eg – Lipo polysaccharides ,

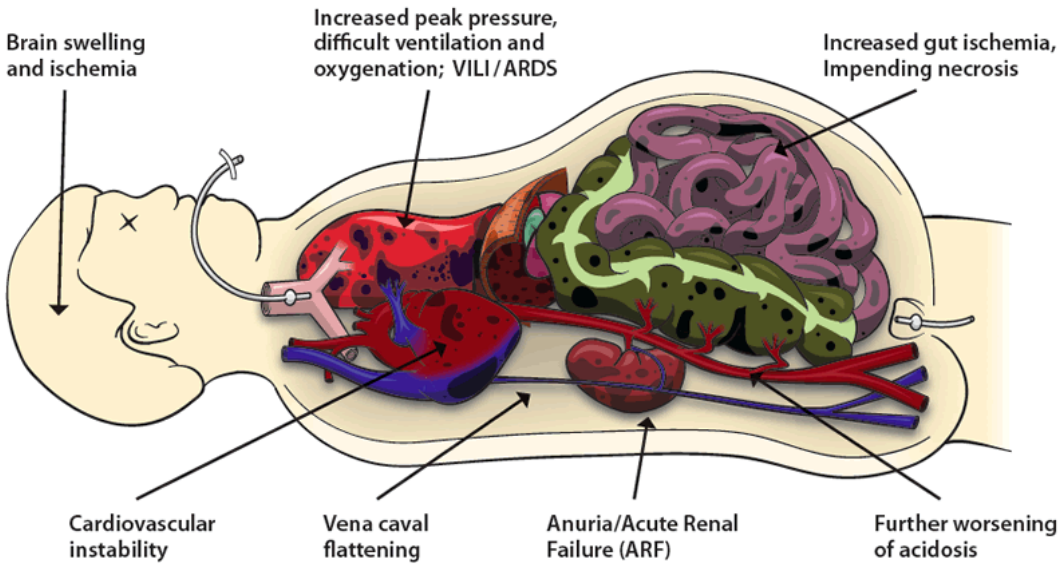
peptide glycans) and host factors (innate & adaptive immunity, endothelial dysfunction)[41,42,43] as shown in the image below.



ORGAN DYSFUNCTION IN SEVERE SEPSIS

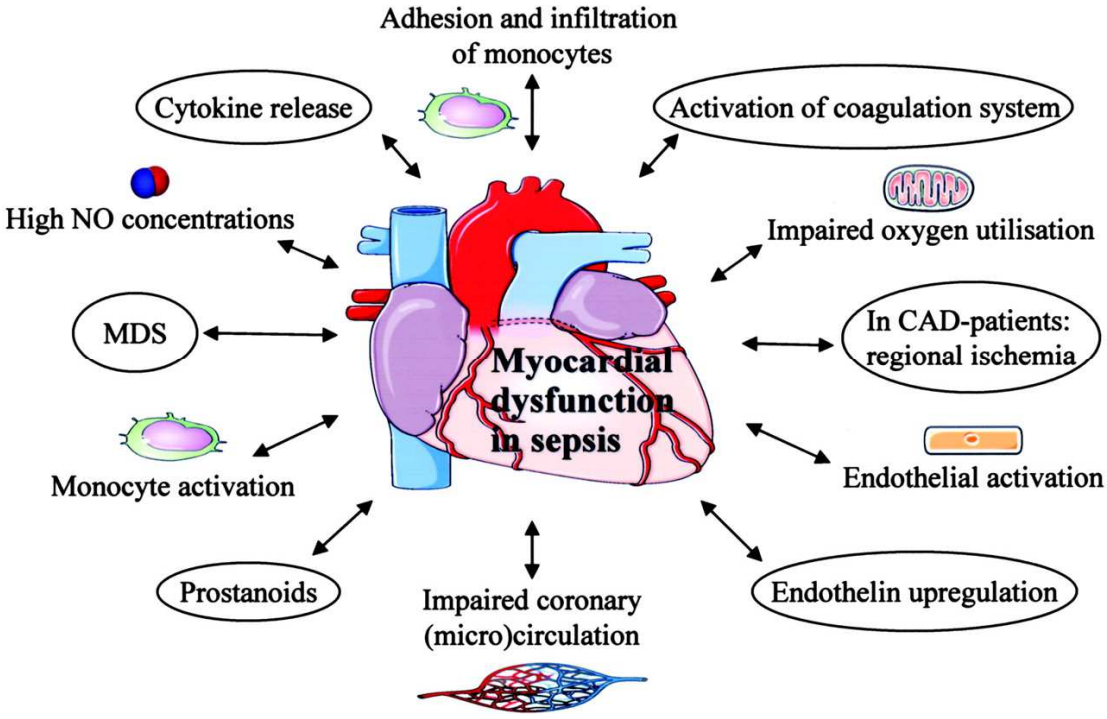
Sepsis exerts a detrimental effect on all the major organ systems in the body including the central nervous system, cardio vascular system, coagulation pathways, gastro intestinal system, renal system, respiratory system and the immune system. Presence of dysfunction of two or more organ systems is called Multi Organ Dysfunction Syndrome (MODS). The onset of MODS is associated with a very high mortality in the range of 30 – 75 % which can rise further upto 90% in the background of immune suppression , resistant organisms , advanced age and comorbid conditions[44,45,46].

SEPSIS -- MULTI ORGAN FAILURE



CARDIO VASCULAR SYSTEM

In the year 1951, Waisbren et al first described the myocardial dysfunction in sepsis. The presence of reduced systemic resistance in sepsis initially masks the reduced myocardial contractility. But with progressive disease there is frank manifestation of the reduced stroke volume and ejection fraction. Onset of cardiovascular dysfunction in sepsis significantly increases its mortality rates. The generalised vaso dilatation, increased capillary permeability and the myocardial depression contribute to a state of tissue hypo perfusion which is reflected by the elevated lactate levels[11].



RENAL SYSTEM

Renal failure occurs in almost 20 % cases of severe sepsis. In fact sepsis is considered to be the most common cause of Acute Kidney Injury (AKI) in the intensive care setup. The conventional tools used in the detection of AKI namely urinary casts and fractional excretion of sodium are insufficient to make an early diagnosis of sepsis related AKI. This has prompted the use of novel bio markers namely Neutrophil Gelatinase Associated Lipocalin (NGAL), cystatin C, urinary interleukin 18 and Kidney injury molecule (KIM 1). Some of these bio markers may even differentiate between septic AKI and non septic AKI.

Sepsis produces AKI through various pathways like direct inflammatory insult, ischemia reperfusion injury, dysregulated coagulation, endothelial cell dysfunction and increased apoptosis. The increased levels of pro inflammatory substances in sepsis like TNF alpha, interleukins and interferons exert a direct toxic effect on the glomerular cells and the renal tubular epithelium. The elevated levels of nitric oxide is responsible for the generalised vaso dilatation with secondary hypotension and activation of the renin – angiotensin axis which triggers a intra renal vasoconstriction leading to fall in glomerular filtration rate. Also the Hypotension, intra vascular hypovolemia, renal vaso constriction and the cytokine storm result in acute tubular necrosis. Thus there is a

multi directional insult to the renal parenchyma necessitating an urgent renal replacement therapy[49,50,51].

Some of the treatment strategies in the treatment of sepsis related AKI are outlined below :

- Volume repletion and vasopressor support to maintain a mean arterial pressure of atleast 65 mm Hg and a central venous pressure of 8-12 mm Hg
- The vasopressors that have been found effective in septic shock are nor epinephrine and vasopressin. They have to be initiated as early as possible in septic shock
- Tight glucose control using regular insulin
- Fenoldopam , a dopamine agonist has been shown to improve renal blood flow and can be tried
- Activated protein C can reduce the thrombin load and thus modulate the endothelial dysfunction
- N acetyl cysteine and Atrial Natriuretic Peptide have been shown to have benefit in septic AKI
- Novel therapeutic approaches include use of TLR inhibition , suppression of the inducible nitric oxide synthase pathways ,

caspase inhibitors , lysophosphatidic acid and use of mesenchymal stem cells

- Early initiation of extra corporeal purification of blood which has the added advantage of removal of excess cytokines
- Hemofiltration , hemadsorption and renal assist devices have been tried[52,53,54]

CENTRAL NERVOUS SYSTEM

Many cases of severe sepsis develop a septic encephalopathy which may manifest as delirium, confusional states and coma.

The factors contributing to the development of this septic encephalopathy include

a) disruption of the blood brain barrier
b) intra cranial hemorrhage (due to DIC)
c) micro infarcts
d) hypoxic encephalopathy
e) cytokine excess and
f) development of metastatic abcesses

The septic encephalopathy can lead to long term residual neurological sequelae. These patients are also prone to develop critical illness polyneuropathy due to the sensori motor axonal degeneration and this entity is characterised by hypotonic limbs and diminished

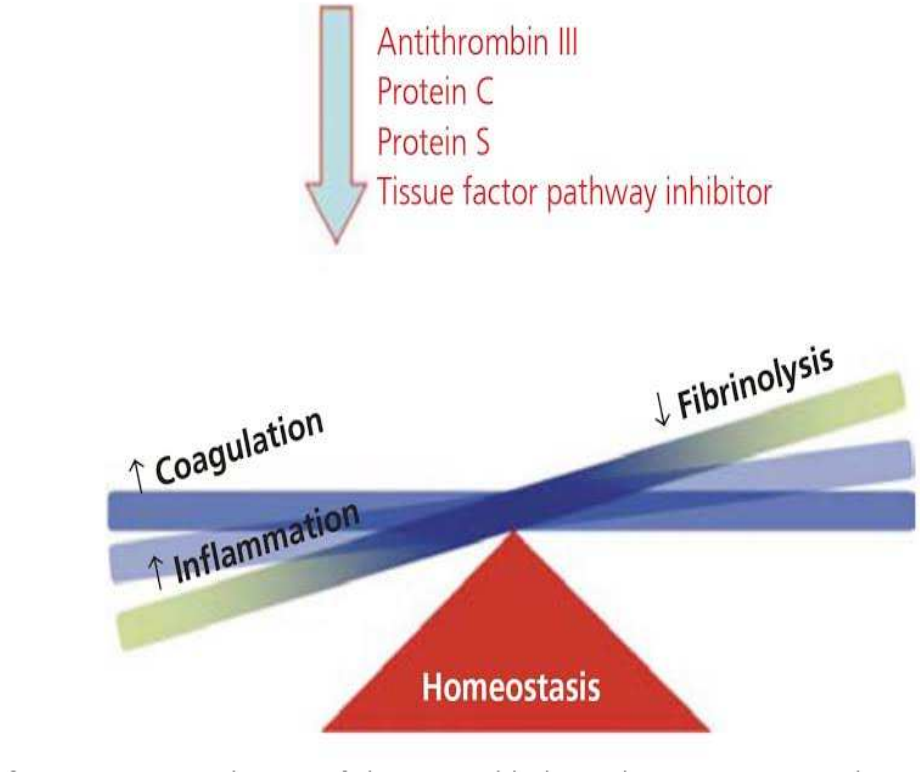
reflexes[55,56]. The psychological impact of ICU stay in the form of depression and anxiety neuroses are also to be borne in mind.

GASTRO INTESTINAL SYSTEM

Severe sepsis results in hypotension which may result in reduced perfusion pressures in the splanchnic circulation thereby inducing liver dysfunction. It can also cause bacterial translocation from the gut and endotoxemia. Usually these translocated bacteria and the bacterial products would be destroyed by the reticulo endothelial system of the liver[57,58]. But on account of the hepatic ischemia in sepsis these toxins directly enter the systemic circulation and exert their inflammatory effects.

COAGULATION PATHWAYS

An imbalance occurs between the pro thrombotic and anti thrombotic substances[59,60] , as shown in the following picture



Coagulation pathways are more likely to be affected in gram negative sepsis where the endothelial dysfunction is more pronounce leading on to disseminated intravascular coagulation (DIC). This is a consumptive coagulopathy with presence of both thrombotic and hemorrhagic manifestations. It can predispose to the development of micro angiopathic hemolytic anemia (MAHA) , acute renal failure and intra cranial hemorrhages and infarcts.

IMMUNE DYSFUNCTION

Sepsis can dysregulate the immunological pathways through the cytokine storm thereby producing a state of relative immuno suppression[61].

CUTANEOUS MANIFESTATIONS

Sepsis, either directly or via disseminated intra vascular coagulation can produce skin lesions like petechiae, purpurae, vesicles, blisters, necrosis and gangrene. The dermis is affected due to the disruption of its blood vessels by the micro thrombi. A cutaneous necrotic hemorrhagic lesion called purpura fulminans is particularly common in septicemia caused by Neisseria meningitidis and streptococcus pneumoniae.

Musher said that there are mainly three patterns of involvement of the skin in Gram negative sepsis.

1) Cellulitis and thrombophlebitis
2) Ecthyma gangrenosum in cases of impaired inflammatory response due to neutropenia
3) Symmetrical peripheral gangrene associated with disseminated intra vascular coagulation[62].

Palpable petechiae and purpurae may also be due to leukocytoclastic vasculitis associated with organisms like Neisseria, pneumococci and staphylococcus aureus. A diffuse erythematous picture termed *erythroderma* may occur in toxic shock syndrome caused by staphylococcus aureus or streptococcus pyogenes. Desquamation of the skin may occur after two weeks.

RESPIRATORY SYSTEM

Often the earliest evidence of sepsis is hyperventilation with respiratory alkalosis. There is alveolar and interstitial fluid accumulation along with increase in the inflammatory cells and cytokines. This produces a disruption of the alveolar membrane. Also there is proliferation of the Type II pneumocytes which replaces the Type I cells with associated surfactant deficiency. Progressive alveolar exudates, interstitial fluid accumulation and the fibrotic changes predispose to the Acute Respiratory Distress Syndrome (ARDS) [63].

ARDS is characterised by the presence of the following components

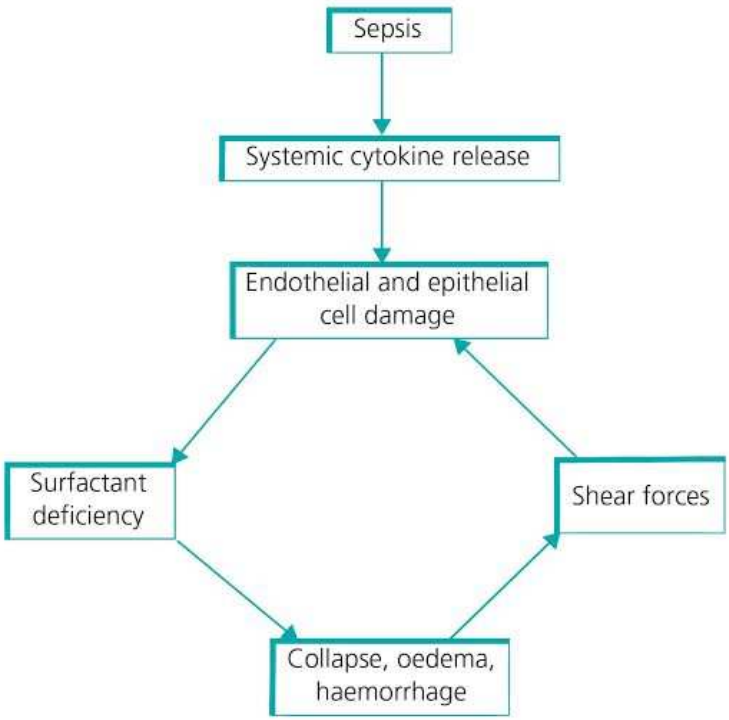
I. Onset of a lung injury within one week of the known clinical insult
II. Bilateral opacities on chest X ray
III. Absence of cardiac failure related fluid overload
IV. Presence of hypoxemia

The term *acute lung injury* has been replaced by the newer Berlin definitions of varying grades of ARDS. This grading system is based on the pAO2 / FiO2 ratios.

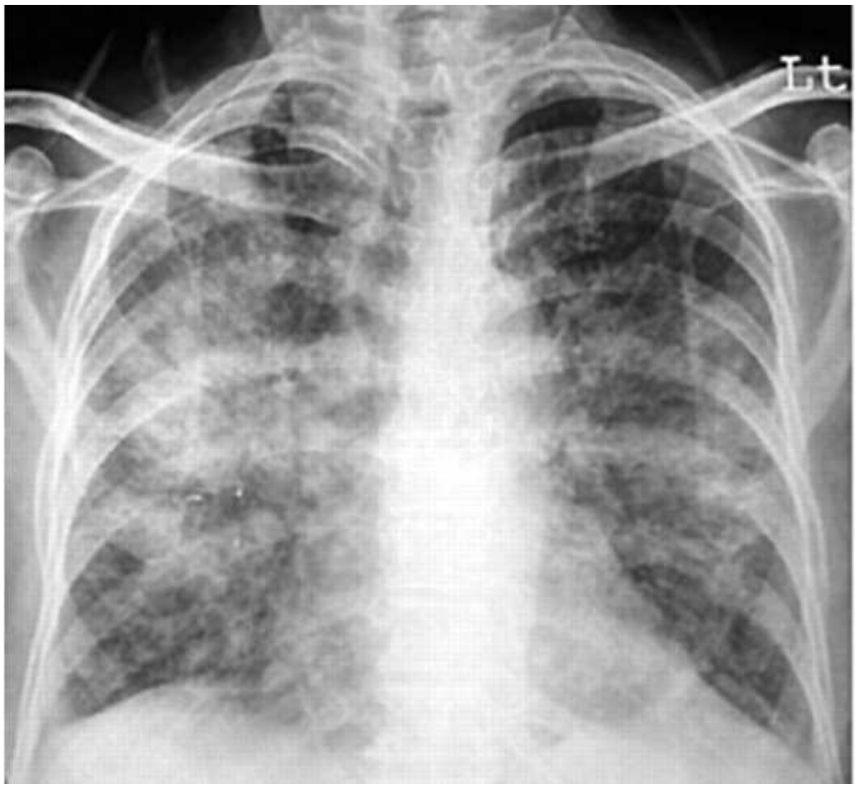
Thus ARDS is categorised as

1. Mild ARDS - pAO2 / FiO2 : 200 to 300
2. Moderate ARDS - pAO2 / FiO2 : 100 to 200
3. Severe ARDS - pAO2 / FiO2 : < 100

SEPSIS – ARDS PATHWAY



CHEST X RAY – ARDS



INVESTIGATIONS TO BE DONE IN SEPSIS

The investigations are done to assess the following factors

1. Source of infection
2. Severity of infection (especially the organ dysfunction)
3. Causative micro organisms
4. Prognostication

Firstly the basic investigations are done. The complete blood count shows evidence of sepsis in the form of leucocytosis or cytopenias. The serial monitoring of cell counts often gives an idea about the response to treatment.

Typically these septic conditions have neutrophilic leucocytosis. However certain infections like typhoid , brucellosis , Rocky mountain spotted fever, ehrlichiosis etc may present with peripheral blood leukopenia[64].

The liver function tests, renal function tests , coagulation profile and arterial blood gas analysis throw light on the presence and extent of organ dysfunctions. Often, unexplained hyperbilirubinemia, hyper lactatemia, metabolic acidosis, respiratory alkalosis or a thrombocytopenia are the earliest evidences of a septic process. Imaging modalities (chest X ray, X ray- paranasal sinuses, ultrasound of abdomen , CT and MRI imaging of relevant areas , echocardiography) are very useful in localising the source of infection. Cytokine and bio marker assay may be done if the facilities are available.

Before starting the antibiotics blood cultures and cultures of relevant tissue or fluids (including pus, sputum, CSF, urine, stool, bone marrow, skin lesions) are to be taken. The blood cultures are to be taken

from two or three different venipuncture sites. The volume of each blood culture sample should be atleast 23 – 30 ml. These indicate the etiological agents involved and their drug sensitivities. Microscopic examination of the infected fluids or tissue samples and staining with Gram stain / AFB stain may also be done. Molecular assays like the polymerase chain reaction methods are useful.

Acute phase reactants like C Reactive Protein (CRP) , procalcitonin and the erythrocyte sedimentation rate (ESR) are useful in gauging the severity of sepsis and its response. Baseline serum cortisol and ACTH levels are useful in the diagnosis of critical illness associated adrenal insufficiency[65,66,67,68].

Assessment of the prognosis in severe sepsis is important to both the physician and the patients since they help in better decision making. Serum lactate levels and serum pro calcitonin are particularly useful in this regard. Prognostic scores have been developed based on some of the commonly used blood investigations and clinical parameters to guide the health care personnel.

DIFFERENTIAL DIAGNOSIS OF SEPSIS

Many conditions can produce a state of hypotension , raised body temperature and evidence of multi organ dysfunction and thus mimic sepsis. Some of these conditions are listed below :-

1. Burns
2. Trauma
3. Adrenal insufficiency
4. Pancreatitis
5. Pulmonary embolism
6. Occult internal bleed
7. Cardiac tamponade
8. Drug overdose or drug reaction
9. Ruptured or dissecting aneurysm of aorta
10. Thyroid storm
11. Serotonin syndrome
12. Heat stroke
13. Anaphylaxis
14. Post cardio pulmonary bypass
15. Malignant hyperthermia[69,70]

MANAGEMENT OF SEPSIS

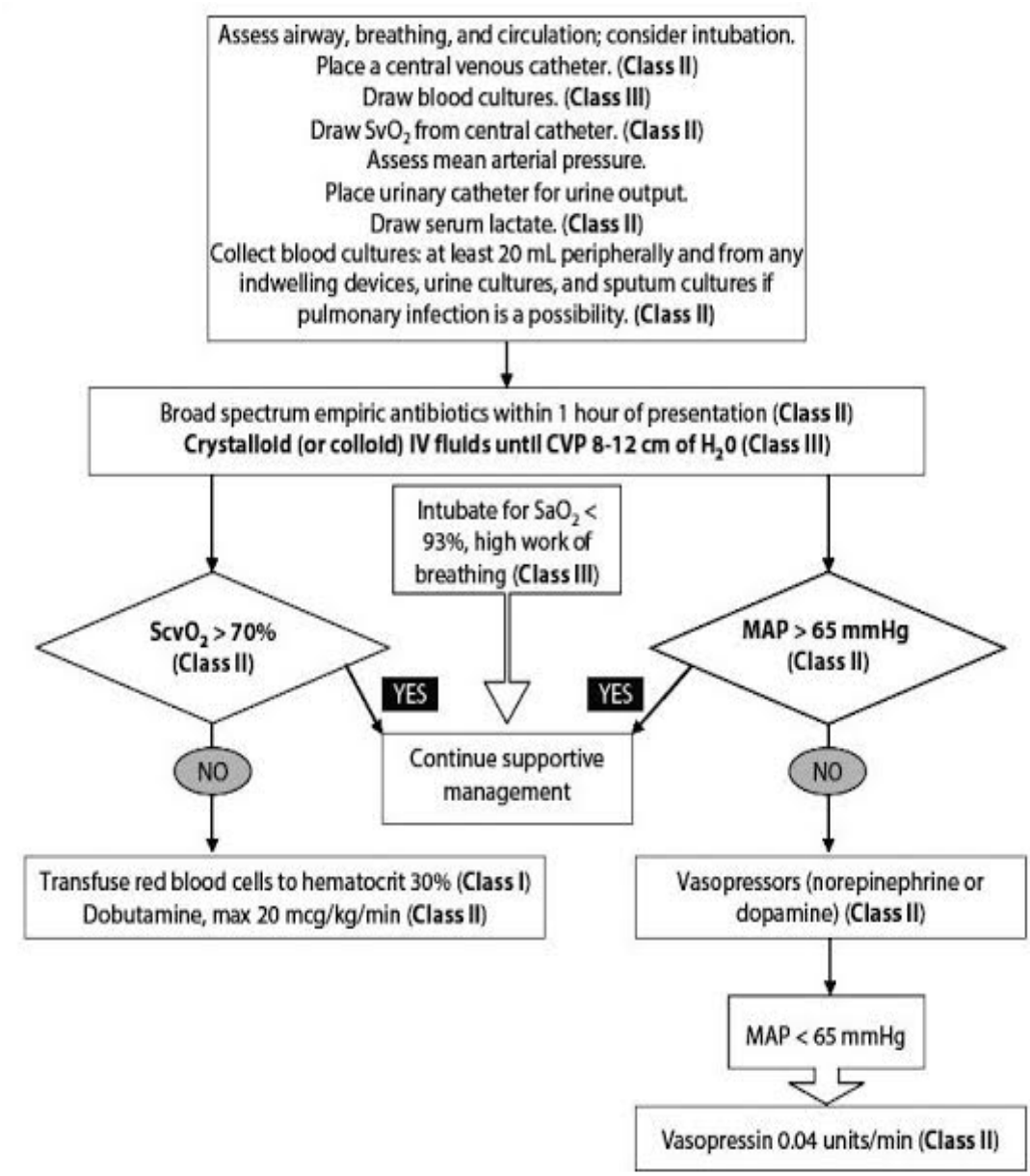
INITIAL RESUSCITATION

Adequate IV fluids have to be give to maintain targets of

1. Central venous pressure 8-12 mm Hg
2. Mean arterial pressure > 65 mm Hg
3. Venous oxygen saturation > 70 %
4. Urine output > 0.5 ml / kg / hr
5. Normalisation of lactate levels

The best fluids for the initial resuscitation are crystalloids. An initial fluid challenge of about 15 – 30 ml / kg may be cautiously given. Further fluids may be given as per the hydration status , vitals and urine output. If the blood pressure fails to pick up despite adequate fluid resuscitation , vasopressors and inotropes are considered. Blood products may be transfused to maintain a hemoglobin concentration of atleast 7 to 9 gm %. A platelet count of < 10,000 per cu mm warrants platelet transfusion. If surgery is contemplated a higher platelet count of around 50,000 / cu mm is to be maintained[71,72.73].

The algorithm for the initial resuscitation in a case of severe sepsis is depicted in the following picture.



NUTRITIONAL SUPPORT

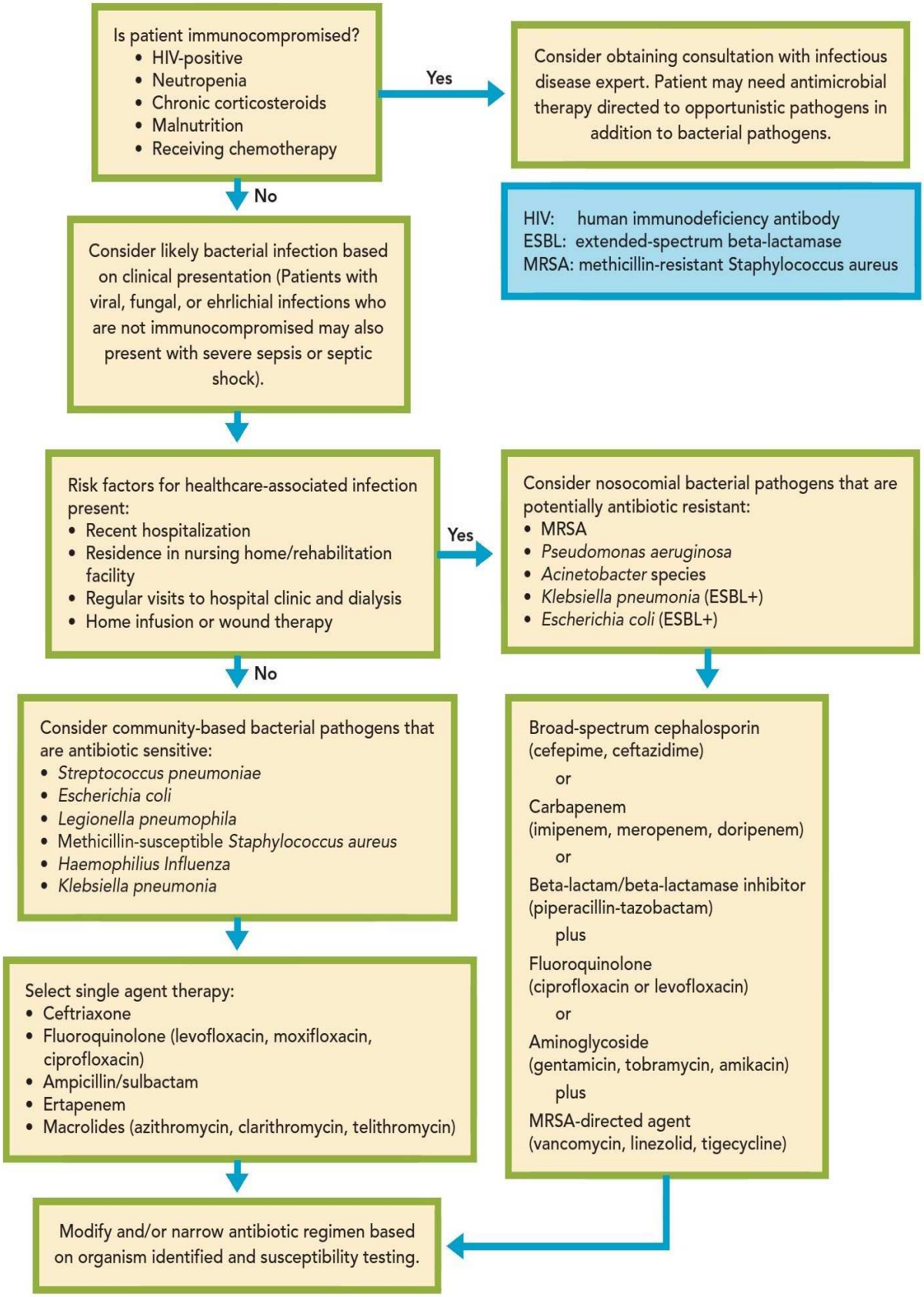
Adequate calories should be replenished as per the body weight of the patient. Enteral route is to be preferred[74,75].

ANTI BIOTICS

Effective empirical anti microbial agents against all of the presumed causative organisms (bacterial , viral and fungal as per the clinical scenario) are to be started. The agents that have good penetration into the tissues that are suspected to be the source of infection are chosen. Combination of empirical agents can be used especially in immuno compromised and neutropenic patients. The empirical therapy is given only till the availability of the culture sensitivity report after which the specific antbiotics are instituted.

Ideally these antibiotics are given for a a period of 7 – 14 days.

AN ALGORITHM FOR ANTIBIOTIC PROTOCOL IN SEPSIS



SOURCE CONTROL

The anatomical location of the source of infection is made out as early as possible. If it is a closed space infection, surgical removal of the infected tissues and fluids are to be considered. Any long standing indwelling vascular and other catheters are to be removed[76,77].

The doses and effects of important drugs used in the management of severe sepsis are mentioned in the following table.

I. Vasopressors		CO	MAP	SVR
Norepinephrine	0.05–0.5 μg/kg/min	–/+	++	+++
Dopamine	5–20 μg/kg/min	++	+	++
Epinephrine	0.05–2 μg/kg/min	++	++	+++
Phenylephrine	2–10 μg/kg/min	0	++	+++
Vasopressin	0.04 units/min	0	+++	+++
II. Inotrope				
Dobutamine	2.5–10 μg/kg/min	+++	–/+	–/0
III. Drotrecogin alfa (activated)	24 μg/kg/hr for 96 hr			
IV. Corticosteroids				
Hydrocortisone (+/– fludrocortisone 50 μg daily)	50 mg every 6 hr			

Key : CO-cardiac output , MAP – mean arterial pressure ,

SVR – systemic venous return

ROLE OF STEROIDS

Severe sepsis with shock that is unresponsive to iv intra venous fluids and vasopressors may respond to parenteral hydro cortisone[78].

MANAGEMENT OF ARDS

ARDS is ideally managed with mechanical ventilation with following points kept in mind

1. A low tidal volume of around 6 ml / kg is preferred
2. Plateau airway pressures should be < 30 cm H_2O
3. Higher PEEP is to be used to prevent alveolar collapse
4. Recruitment manoeuvres and prone positioning have been reported to have improved outcomes in studies[79]

GLYCEMIC STATUS

A good glycemic status, targetting a sugar level of < 180 mg / dl is needed for a better control of sepsis[80,81]

DIALYSIS

Since patients with severe sepsis are prone to develop acute kidney injury (AKI) at some point in the course of the disease , a renal replacement therapy will be needed[82]

DVT PROPHYLAXIS

Patients with severe sepsis should be treated with daily small dose of low molecular weight heparin to prevent the occuerrence of deep

venous thrombosis (DVT). Caution is to be exercised while prescribing these low molecular weight heparin to a patient with a creatinine clearance of < 30 ml/min. If the patient has documented hypersensitivity to heparin, other options like compression stockings , intermittent pneumatic compression devices etc may be considered[83].

STRESS ULCER PREVENTION

Cases of severe sepsis should receive prophylaxis against the development of stress ulcers especially if there is a tendency to bleed. The proton pump inhibitors like pantoprazole are preferred to histamine receptor blockers in this regard.

MONITORING THE ORGAN FUNCTION

Throughout the course of treatment, the organ function parameters are to be monitored and this gives an idea about the severity of sepsis and also about the dose reduction of the medications. The following chart lists the parameters that are to be monitored during treatment[84]

Organ system	Parameter
Respiratory system	PaO2/FiO2 ratio
Renal system	Urine output and serum creatinine
Hematologic system	Platelet count
Central nervous system	Glasgow coma score
Hepatobiliary system	Serum bilirubin and liver enzymes
Cardiovascular system	Blood pressure, arterial lactate
Gastrointestinal system	Gastric intramucosal pH (pHi), ileus, blood in nasogastric aspirate

RISK PROGNOSTICATION IN SEPSIS

Many scoring systems have been developed to predict the severity, prognosis and risk of in-hospital mortality in critically ill patients including those suffering from severe sepsis. These models provide information regarding the degree of functional derangements in the various organs and the likelihood of serious morbidity and mortality. They usually have two parts – a score and a mortality assessment based on the score. The usual variables taken into account are age, comorbidities, functional derangements of organs , use of interventions and admission diagnosis. Such prognostic scores enable the physicians and hospital administrators to improve their decision making skills. They also help in better allocation of hospital resources[85,86,87].

Some of these scores are

1. APACHE II {Acute Physiology and Chronic Health Evaluation } Score
2. SAPS { Simplified Acute Physiology } Score
3. SOFA {Serial Organ Failure Assessment } Score
4. MPM { Mortality Prediction Model}

Based on their development , these scoring systems may be categorised into generations as shown below

First generation:	Second generation
APACHE I	APACHE II
	SAPS I
	MPM I
Third generation	Fourth generation
APACHE III	APACHE IV
SAPS II	SAPS III
MPM II	MPM_0 III

Usually the data that are objective, highly reproducible and those that are easy to measure are used in these scoring systems. Based on these data and associated equations the risk scores are calculated and then the patients may be stratified into varying levels of risk groups.

There are five important uses of such scoring systems

i. To measure the severity of disease and thereby enable the health care providers to make decisions regarding resource allocation
ii. The ICU performances of various ICU s can be compared using these scoring systems
iii. Such scores are utilised in randomised controlled trials
iv. The prognosis can be explained to patient relatives objectively
v. These are also used to assess whether the patient is suitable for novel therapeutic measures.

REQUISITES FOR A GOOD PROGNOSTIC SCORING SYSTEM

A good scoring system must be

- Simple
- Easy to use
- Universally applicable
- Reliable and consistent
- Good sensitivity and specificity

Of the various scoring systems that are used in the critically ill patients , there are two that have been tested in many studies and found to be effective prognosticatory tools. They are the APACHE II and SOFA scores.

APACHE II SCORE

The APACHE II or the Acute Physiology And Chronic Health Evaluation Score was first developed by the US researchers led by Knaus et al. The model has been upgraded thrice following British and Irish studies and thus APACHE I , II and III are available. Of these the APACHE II has the advantages of simplicity and effectiveness. This score ranges from 0 to 71 and includes weightage for age , past comorbid conditions and acute physiological parameters[88]. The following 12 parameters are to be taken within the first 24 hours of presentation

i. Temperature

ii. Mean arterial pressure

iii. Heart rate

iv. Respiratory rate

v. pAO2

vi. arterial pH or serum bicarbonate

vii. serum potassium

viii. serum sodium

ix. serum creatinine

x. hematocrit

xi. white blood cell count

xii. Glasgow coma scale

In general the following cases are not to be scored using the APACHE II system

- Age of admission < 16 years
- Duration of stay in the ward < 8 hours
- If the admission is for primary burns
- Admission following coronary bypass grafting
- If the twelve variables within first 24 hours are not available

The method of calculation of the APACHE II score is shown in the subsequent table.

APACHE II SCORE CALCULATION CHART

Physiologic Variable	High Abnormal Range					Low Abnormal Range				
	+4	+3	+2	+1	0	+1	+2	+3	+4	Points
Temperature - rectal (°C)	≥41°	39 to 40.9°		38.5 to 38.9°	36 to 38.4°	34 to 35.9°	32 to 33.9°	30 to 31.9°	≤29.9°	
Mean Arterial Pressure - mm Hg	≥160	130 to 159	110 to 129		70 to 109		50 to 69		≤49	
Heart Rate (ventricular response)	≥180	140 to 179	110 to 139		70 to 109		55 to 69	40 to 54	≤39	
Respiratory Rate (non-ventilated or ventilated)	≥50	35 to 49		25 to 34	12 to 24	10 to 11	6 to 9		≤5	
Oxygenation: A-aDO2 **or** PaO2 (mm Hg) a. FIO2 ≥0.5 record A-aDO2 b. FIO2 <0.5 record PaO2	≥500	350 to 499	200 to 349		<200 PO2>70	 PO2 61 to 70		 PO2 55 to 60	 PO2<55	
Arterial pH (preferred) Serum HCO3 (venous mEq/l) (not preferred, but may use if no ABGs)	≥7.7 ≥52	7.6 to 7.69 41 to 51.9		7.5 to 7.59 32 to 40.9	7.33 to 7.49 22 to 31.9		7.25 to 7.32 18 to 21.9	7.15 to 7.24 15 to 17.9	<7.15 <15	
Serum Sodium (mEq/l)	≥180	160 to 179	155 to 159	150 to 154	130 to 149		120 to 129	111 to 119	≤110	
Serum Potassium (mEq/l)	≥7	6 to 6.9		5.5 to 5.9	3.5 to 5.4	3 to 3.4	2.5 to 2.9		<2.5	
Serum Creatinine (mg/dl) Double point score for acute renal failure	≥3.5	2 to 3.4	1.5 to 1.9		0.6 to 1.4		<0.6			
Hematocrit (%)	≥60		50 to 59.9	46 to 49.9	30 to 45.9		20 to 29.9		<20	
White Blood Count (total/mm3) (in 1000s)	≥40		20 to 39.9	15 to 19.9	3 to 14.9		1 to 2.9		<1	
Glasgow Coma Score (GCS) Score = 15 minus actual GCS										
A. Total Acute Physiology Score (sum of 12 above points)										
B. Age points (years) ≤44=0; 45 to 54=2; 55 to 64=3; 65 to 74=5; ≥75=6										
C. Chronic Health Points (see below)										
Total APACHE II Score (add together the points from A+B+C)										

SOFA SCORE

The SOFA or Serial Organ Failure Assessment score is used to monitor the physiological status of a critically ill patient. It provides a picture of the functioning of the organ systems and the rate of failure of the organ[89]s. It is the summation of six different scores , each of which represents an organ system. The organs taken into account for the calculation of SOFA score are as follows :

a) Respiratory system

b) Cardio vascular system

c) Liver

d) Coagulation

e) Renal system

f) Central nervous system

The method of calculation of SOFA score is depicted in the following table

SOFA SCORE CALCULATION CHART

Score points	1	2	3	4
Respiration				
PaO_2/FiO_2	<400	<300	<200	<100
			with respiratory support	with respiratory support
Cardiovascular				
Hypotension*	MAP <70 mmHg	Dopamine ≤5 or	Dopamine >5 or	Dopamine >15 or
		dobutamine in any dose	epinephrine ≤0.1 or	epinephrine >0.1 or
			norepinephrine ≤0.1	norepinephrine >0.1
Liver				
Bilirubin mg/dl	1.2–1.9	2.0–5.9	6.0–11.9	>12.0
Renal				
Creatinine mg/dl	1.2–1.9	2.0–3.4	3.5–4.9	5.0
or urine output			or <500ml/2 4h	or <200ml/24 h
Coagulation				
Platelets $\times 10^3/mm^3$	< 150	< 100	< 50	< 25
Central nervous system				
Glasgow Coma Scale	13–14	10–12	6–9	< 6

* Adrenergic agents administered for at least 1 h (doses are given in µg/kg/min)

The SOFA score can be calculated on serial days and the highest SOFA score as well as mean SOFA score may be assessed. A rise in the SOFA score in the first 24 – 48 hours indicates higher risk of mortality. This score is especially useful in the serial monitoring and prognostication of patients with severe sepsis.

Many studies have been conducted to validate the usefulness of these prognostication criteria. Some of the studies have compared different scoring systems and assessed their effectiveness.

Our study is aimed at comparing two of the most important among these systems – namely the APACHE II score and the SOFA score in the setting of Sepsis – Multi Organ Dysfunction Syndrome.

MATERIALS

AND

METHODS

MATERIALS AND METHODS

Aim And Objectives

To determine and compare APACHE II score and SOFA score as predictors of mortality in patients admitted with sepsis and MODS.

Study Centre

Institute of Internal Medicine, Madras Medical College and Rajiv Gandhi Govt General Hospital, Chennai

Duration of Study

6 months

Study Design

Observational Study (prospective and retrospective)

Sample Size

60 patients

Inclusion Criteria

1 .Patients above 18 years of age

2. Patients with evidence of sepsis and MODS on admission

Exclusion Criteria

1. Patients being treated with immunosuppressant medications
2. Patients having retro viral infection
3. Ante natal patients

Data Collection and Methods

Patients are subjected to history taking , clinical examination and relevant laboratory investigations are done.

Materials and Methods

Patients admitted with sepsis and MODS are selected for clinical study as per inclusion / exclusion criteria. They are subjected to routine blood tests like complete hemogram, renal function tests, serum electrolytes, liver function test and arterial blood gas analysis. In relevant cases imaging studies (USG) and fever profile (blood, urine C/S, WIDAL, MSAT, IgM dengue) are evaluated.

These are done to ascertain the presence of Sepsis – MODS. History regarding the clinical presentation, comorbidities are recorded. Clinical examination will be done. Use of any inotropes, ventilatory support, dialytic interventions are noted as the SOFA score includes them for scoring purposes. APACHE II score is calculated within the first 24 hours. SOFA score is calculated on day 1 and day 3 and the mean SOFA

score is calculated. Patients are followed up for outcome in terms of recovery or mortality at 30 days.

Procedure / Investigation Details

1. Hematocrit
2. White blood cell count
3. Platelet count
4. Sr creatinine
5. Sr bilirubin
6. Arterial blood gas analysis
7. Sr electrolytes
8. Blood , urine C/S
9. Smear for Mp
10. WIDAL
11. MSAT &
12. IgM dengue
13. Chest xray
14. USG abdomen (all above workup are to ascertain sepsis – MODS)

Analysis Plan

SPSS, Epi INFO softwares

Sponsorship

No

Conflict of interest

None

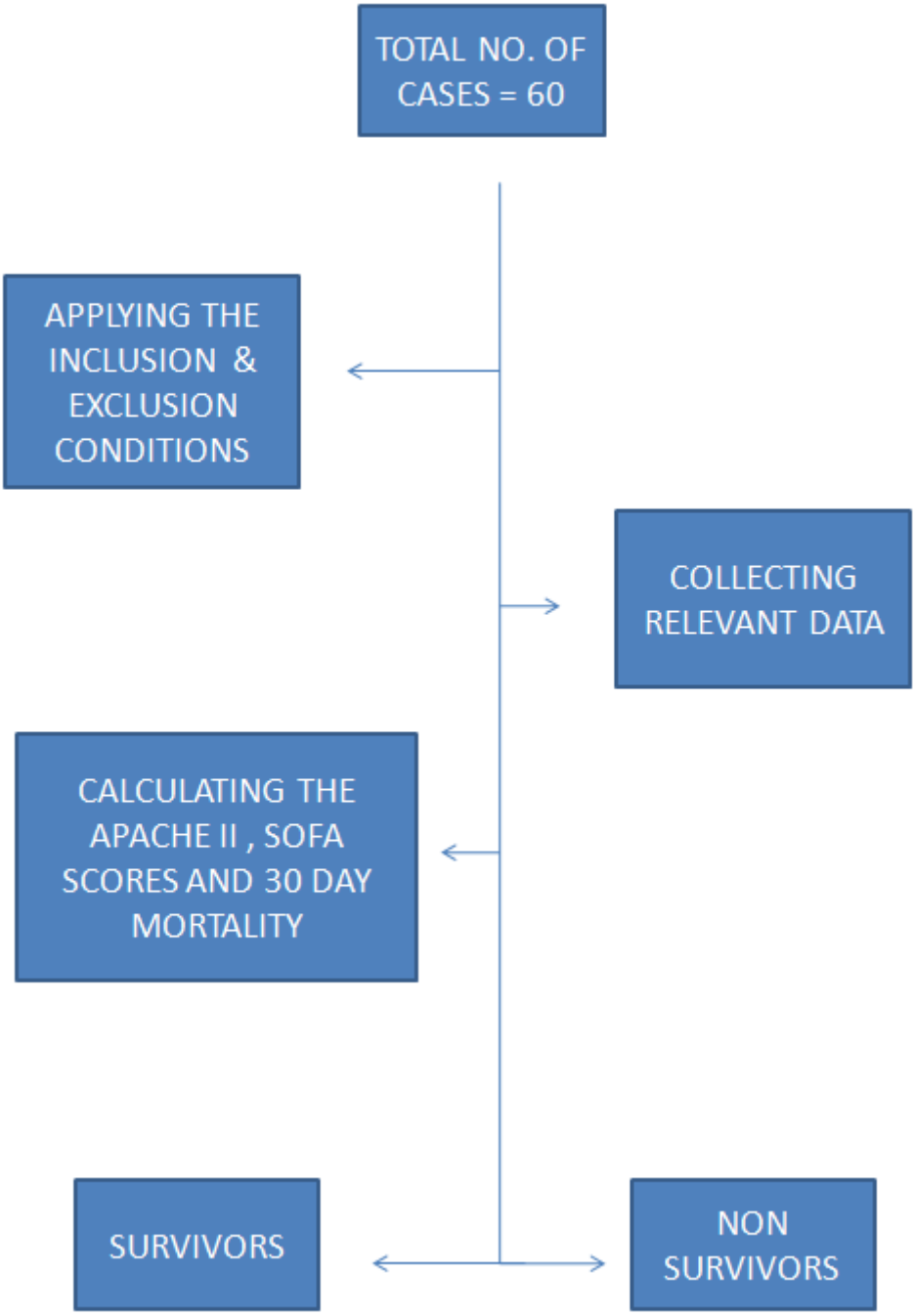
OBSERVATION

AND

RESULTS

OBSERVATION AND RESULTS

FLOW CHART OF THE METHODOLOGY

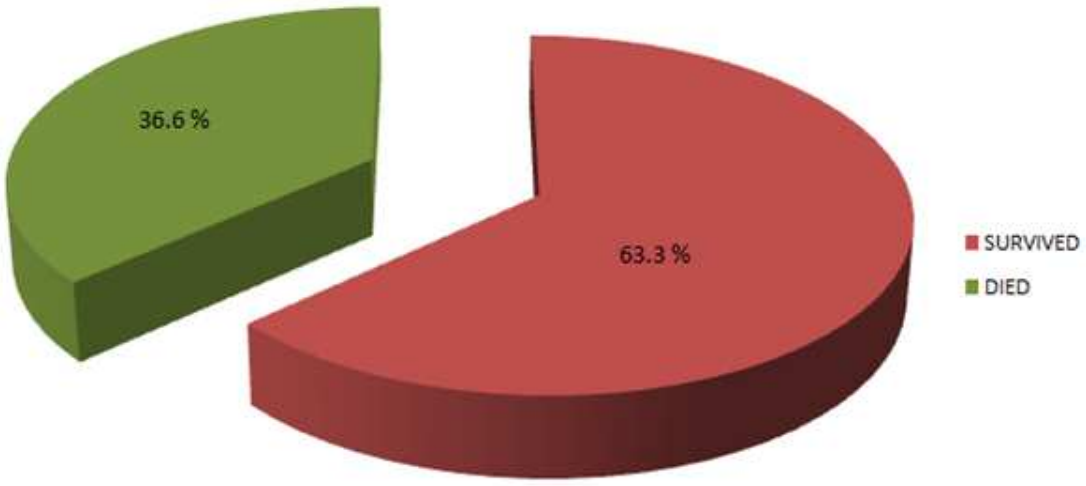


30 DAY MORTALITY RATES IN SEPSIS – MODS IN OUR STUDY

	NUMBER	PERCENTAGE
SURVIVED	38	63.30%
DIED	22	36.60%
TOTAL	60	100%

In our study the mortality rates in patients with Sepsis – Multi Organ Dysfunction Syndrome was found to be 36.6 % which is consistent with several national and international studies which estimate the death rate at 30 – 80 %.

PIE CHART DEPICTING THE MORTALITY IN SEPSIS MODS

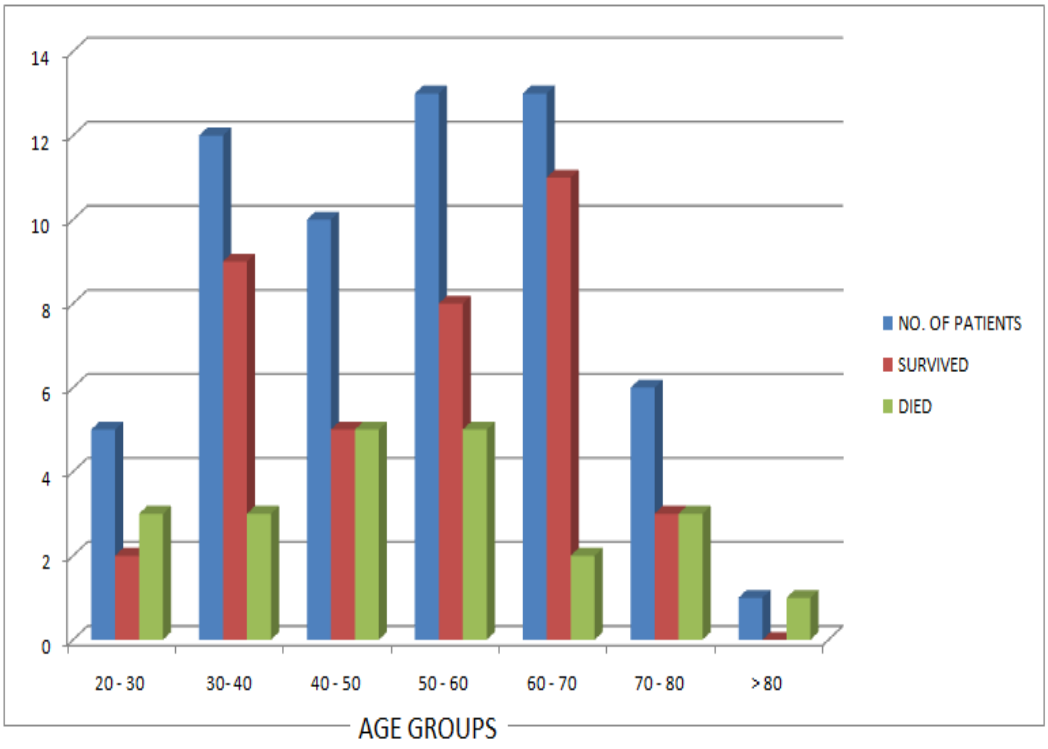


AGE WISE DISTRIBUTION OF SURVIVORS AND NON SURVIVORS

AGE GROUP	NUMBER OF PATIENTS	SURVIVED	DIED	MORTALITY PERCENTAGE
20 – 30	5	2	3	60 %
30- 40	12	9	3	25%
40 – 50	10	5	5	50 %
50 – 60	13	8	5	22.70 %
60 – 70	13	11	2	38.50 %
70 – 80	6	3	3	50 %
> 80	1	0	1	100 %

The majority of deaths were in patients aged above 40 years .

BAR DIAGRAM SHOWING THE AGE WISE DISTRIBUTION OF SURVIVORS AND NON SURVIVORS



AGE -- AS A RISK FACTOR FOR MORTALITY

IN SEPSIS - MODS

PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
AGE	53.02	14.54	51.72	17.53	0.30	*0.38*

The p value being > 0.5 indicates that in our study, the age difference between the survivor group and non survivor group was not significant.

SEX WISE DISTRIBUTION OF SURVIVORS AND NON SURVIVORS

MALE			***FEMALE***		
TOTAL	SURVIVED	DIED	TOTAL	SURVIVED	DIED
31	22	9	29	16	13

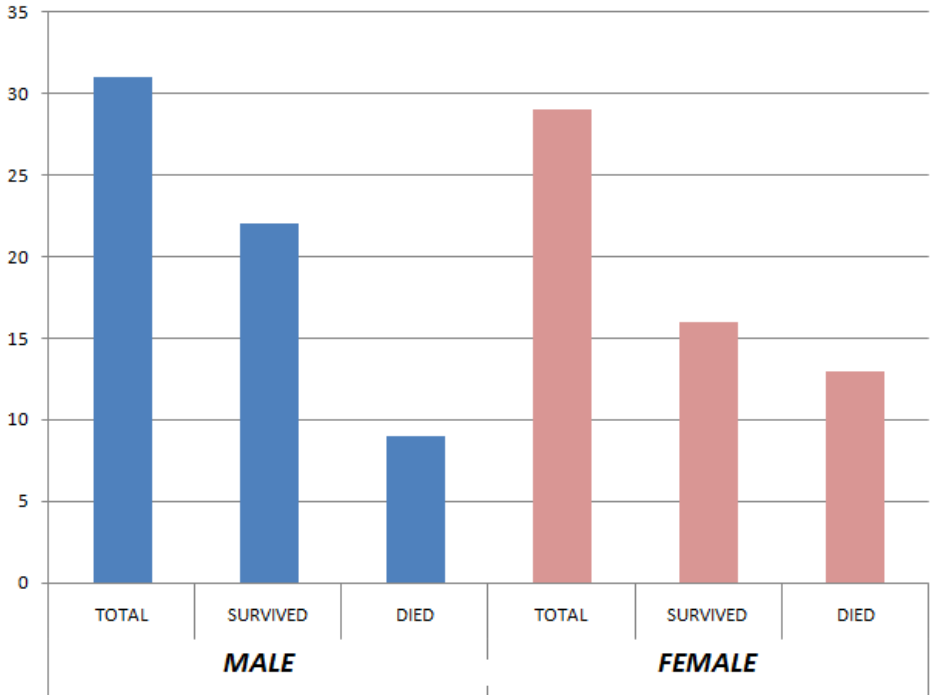
Thus the mortality is noted to be

29.03 % in males and

44.8 % in females

The mortality rates appear to be higher in females than in males.

BAR DIAGRAM SHOWING THE SEX WISE DISTRIBUTION OF SURVIVORS AND NON SURVIVORS



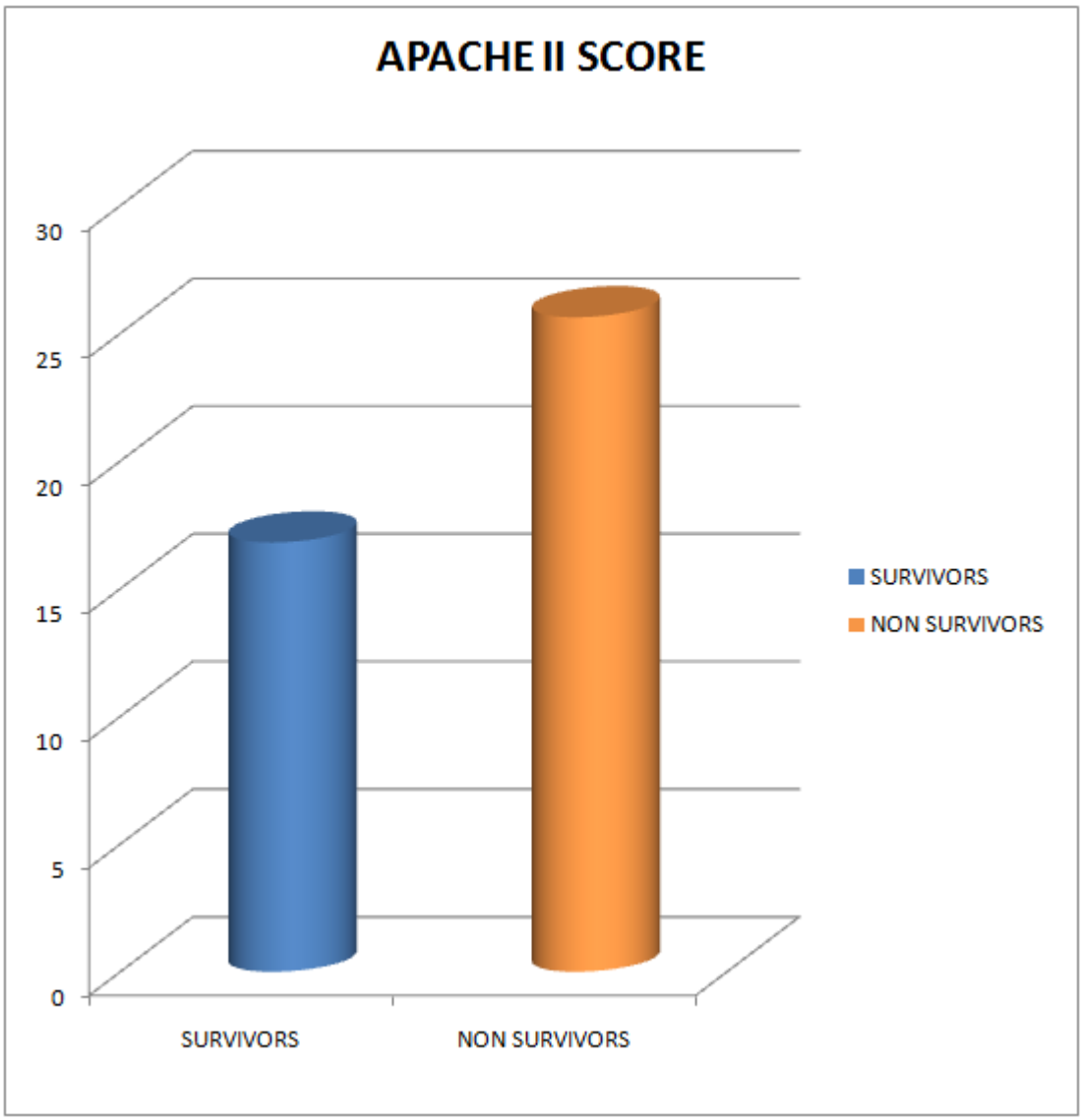
APACHE II SCORE AND ITS CORRELATION WITH 30 DAY MORTALITY

PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
APACHE II SCORE	16.81	4.52	25.63	5.78	6.44	*< 0.05*

P value is significant, implying that APACHE II score (which is measured in the first 24 hours) is a good predictor of 30 day mortality in patients admitted with sepsis – MODS.

The average APACHE II score is noted to be around 16 in survivors but much higher in non survivors (25)

BAR DIAGRAM SHOWING THE CORRELATION BETWEEN APACHE II SCORE AND 30 DAY MORTALITY



SOFA I SCORE AND ITS CORRELATION WITH 30 DAY MORTALITY

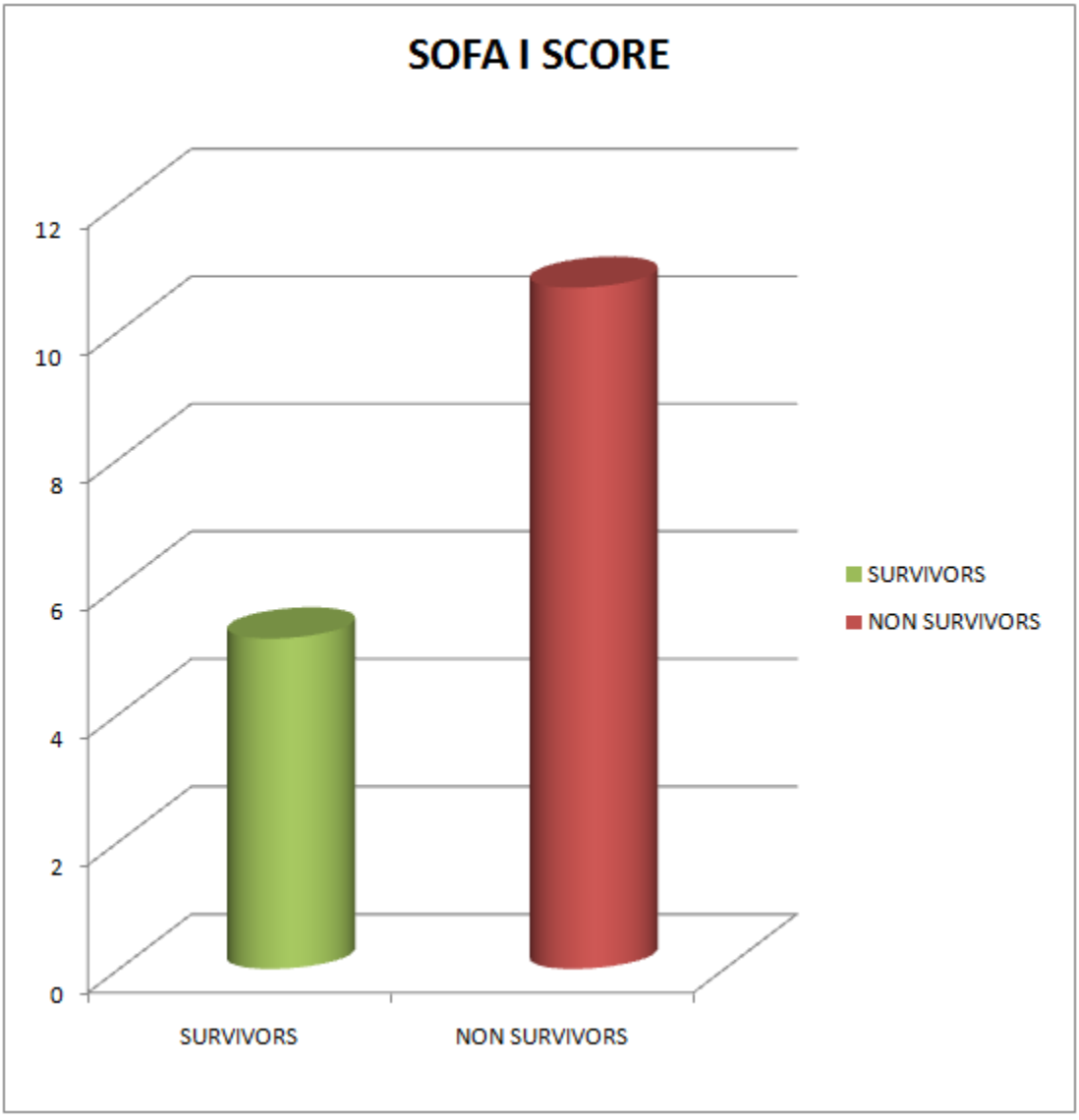
PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
SOFA I SCORE	5.18	1.90	10.68	1.86	9.44	*< 0.05*

SOFA I score refers to the Serial Organ Failure Assessment score derived on the first day of admission.

The above chart shows that SOFA I score has a definite correlation with mortality, since the p value is less than 0.05.

The average SOFA 1 score in survivors is noted to be around 5 while that in non survivors is 10, implying that higher the SOFA 1 score – higher is the mortality.

BAR DIAGRAM SHOWING CORRELATION BETWEEN SOFA I SCORE AND MORTALITY



SOFA III SCORE AND ITS CORRELATION WITH MORTALITY IN SEPSIS – MODS

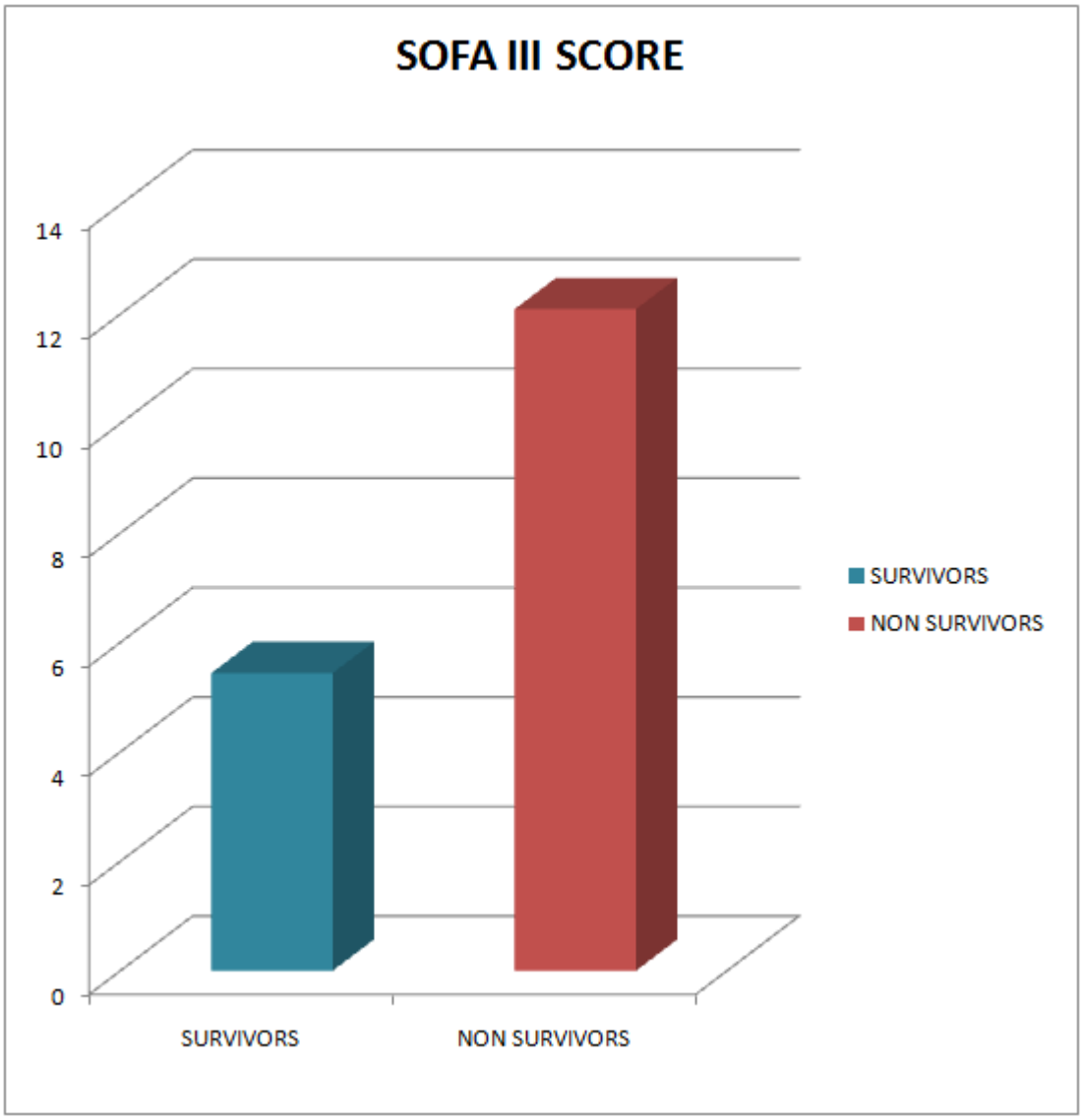
PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
SOFA III SCORE	5.44	1.99	12.09	1.62	13.65	*< 0.05*

Among the twenty two deaths, five had occurred within the first two days and hence the third day SOFA value (SOFA III) could not be obtained.

Leaving out these five cases, the SOFA III score was calculated for the remaining 55 patients in the study group and its correlation with mortality was assessed

As the chart shows the P value was noted to be significant, implying that a higher SOFA III Score is a predictor of mortality

BAR DIAGRAM SHOWING CORRELATION BETWEEN SOFA III SCORE AND MORTALITY



MEAN SOFA SCORE AND ITS CORRELATION WITH MORTALITY IN SEPSIS – MODS

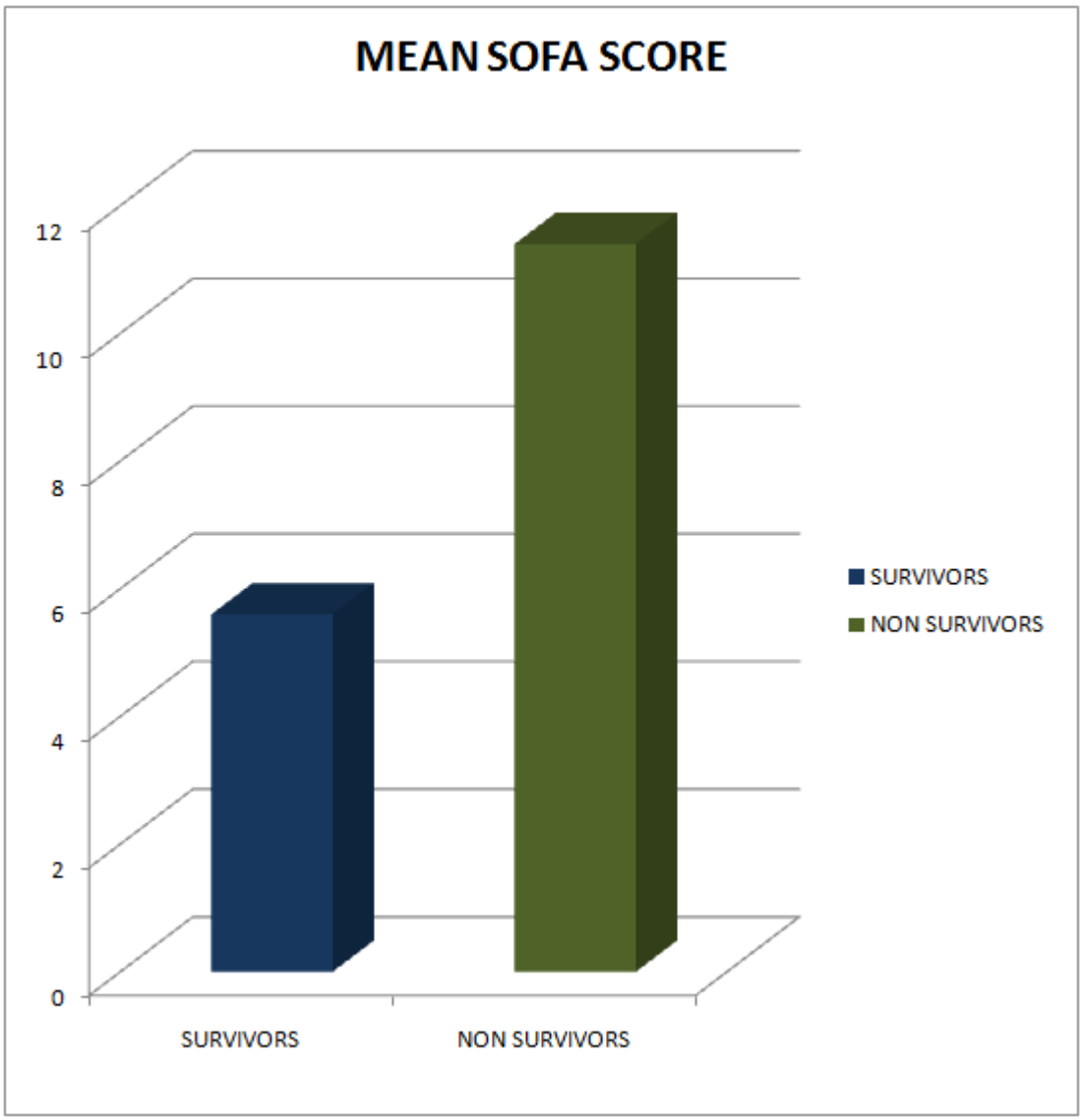
PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
MEAN SOFA SCORE	5.63	1.9	11.38	1.66	11.55	*< 0.05*

Among the patients, for whom a day 1 and day 3 SOFA scores were available , the mean of those two scores were calculated and assessed

The p value was significant

Hence a higher mean SOFA score indicates a higher probability of death

BAR DIAGRAM SHOWING CORRELATION BETWEEN MEAN SOFA SCORE AND MORTALITY

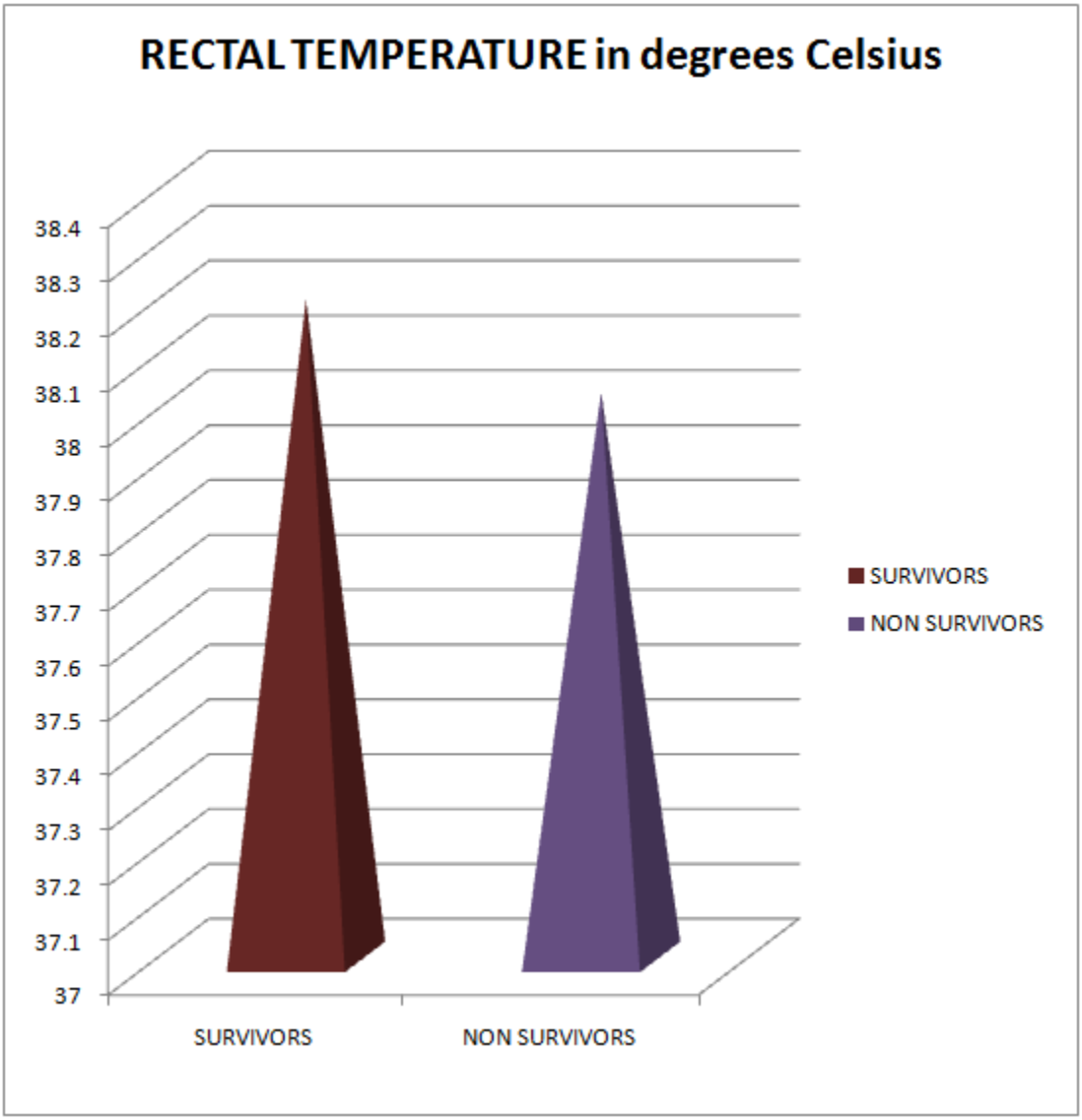


RECTAL TEMPERATURE AND ITS CORRELATION WITH MORTALITY

PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
RECTAL TEMPERATURE In degrees Celsius	38.2	0.69	38.03	0.91	0.77	*0.21*

Here the p value is greater than 0.05 , indicating that rectal temperature has no independent correlation with mortality in patients with sepsis – MODS

BAR DIAGRAM SHOWING THE MEAN RECTAL TEMPERATURE IN SURVIVORS AND NON SURVIVORS



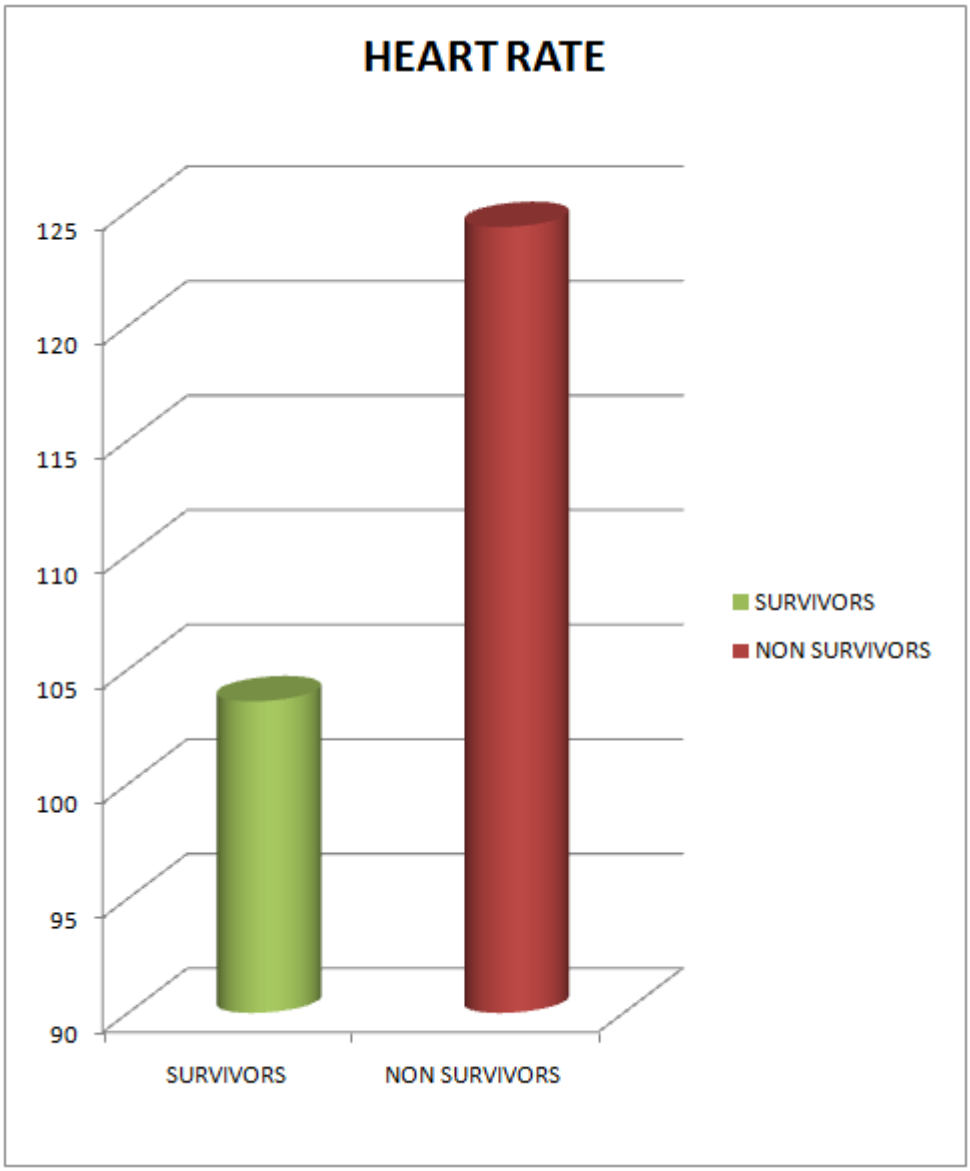
HEART RATE AND ITS CORRELATION WITH MORTALITY

PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
HEART RATE	103.6	22.6	124.3	23.2	3.3	*< 0.05*

There was a positive correlation between heart rate and mortality ($p < 0.0.5$)

The mean heart rate in survivors was 103 while that in non survivors was noted to be higher - 124

BAR DIAGRAM SHOWING THE MEAN HEART RATE IN SURVIVORS AND NON SURVIVORS

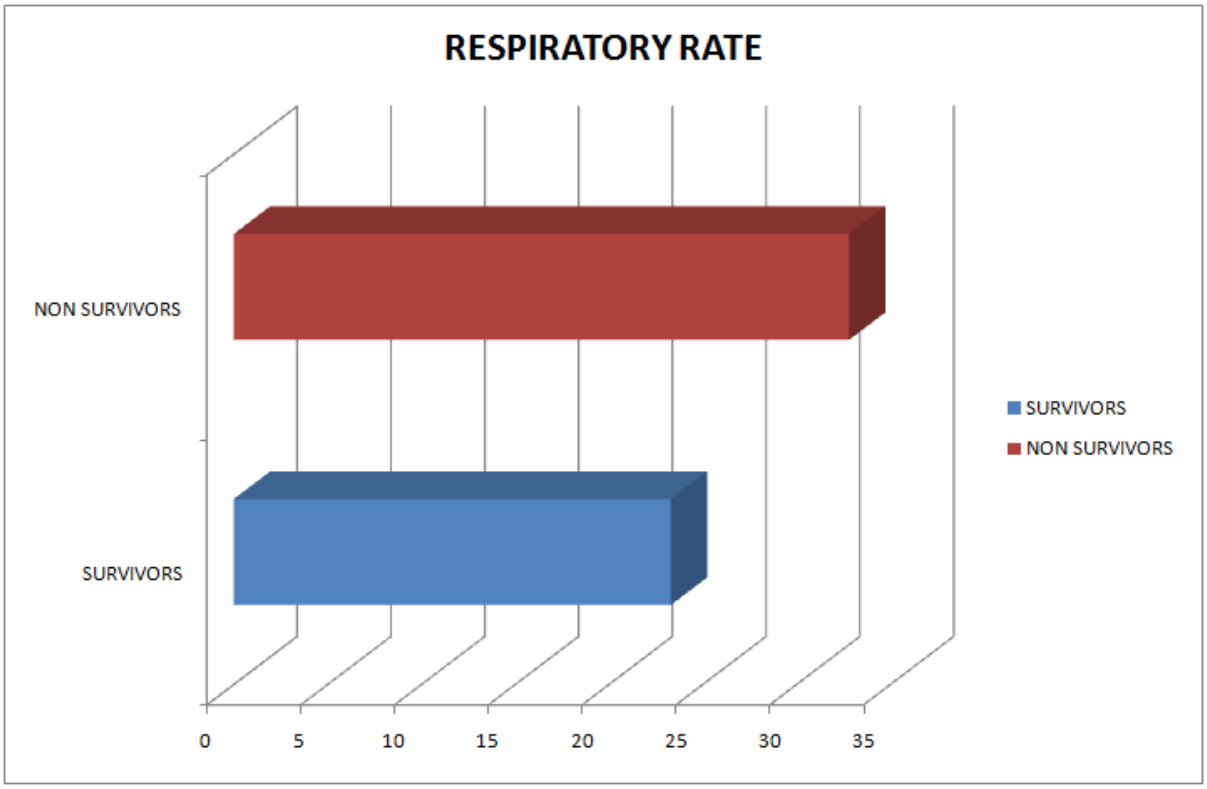


RESPIRATORY RATE AND ITS CORRELATION WITH MORTALITY

PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
RESPIRATORY RATE	23.3	7.5	32.7	7.8	4.6	*< 0.05*

The mean respiratory rate in non survivors was found to be higher in non survivors than in survivors and the p value was also less than 0.05 , suggesting that a higher respiratory rate has an independent correlation with mortality in sepsis – MODS.

DIAGRAM SHOWING THE MEAN RESPIRATORY RATE IN SURVIVORS AND NON SURVIVORS

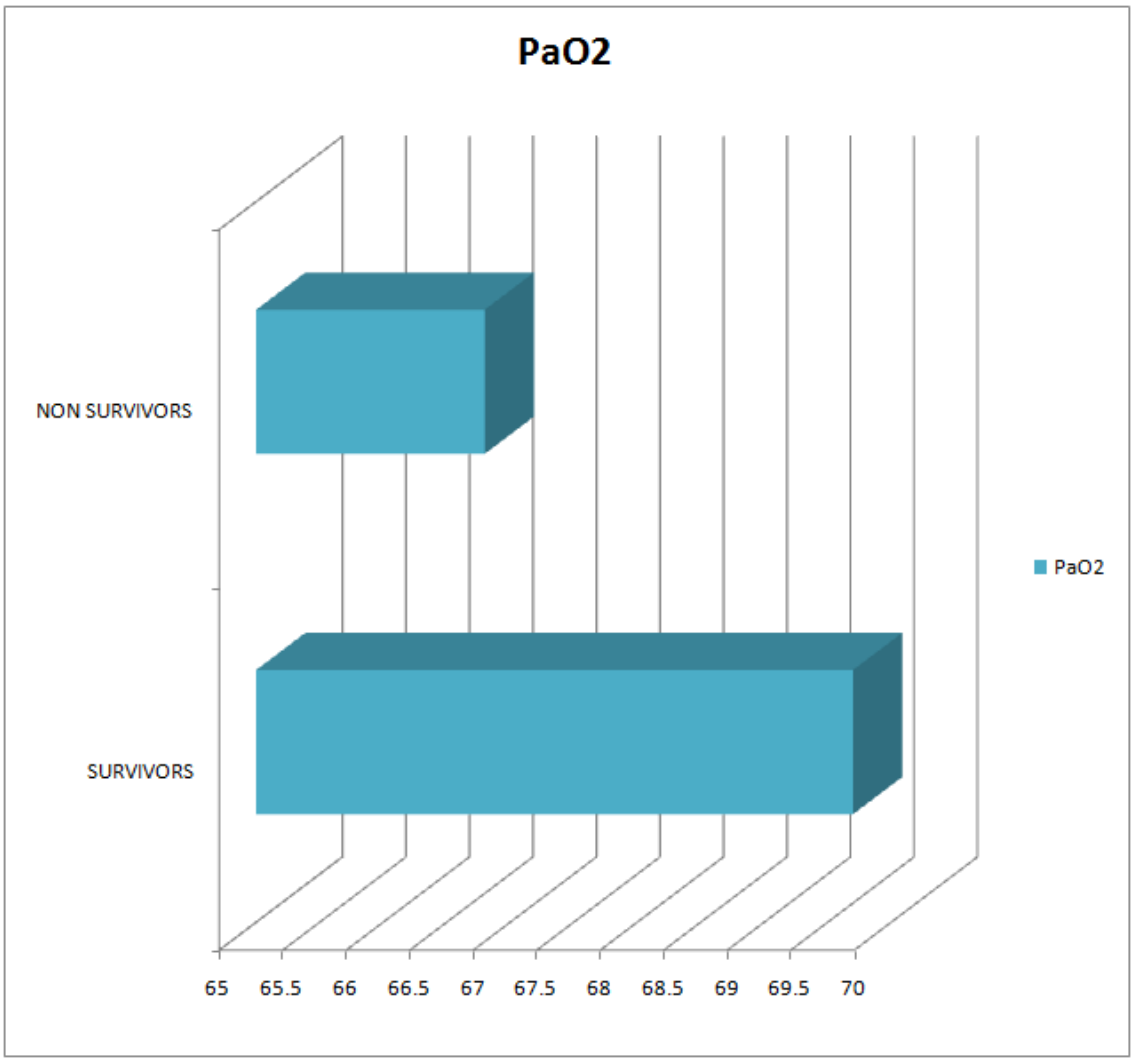


PaO2 AND ITS CORRELATION WITH MORTALITY

PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
PaO2 In mm Hg	69.7	11.26	66.8	11.17	0.94	*0.17*

PaO2 refers to the partial pressure of arterial oxygen. When its values were compared between the survivor group and the non survivor group, it was found that there was no significant relationship between PaO2 and mortality (p value is 0.17 and a value >0.05 is taken as insignificant correlation).

BAR DIAGRAM SHOWING THE MEAN PARTIAL PRESSURE OF ARTERIAL OXYGEN IN SURVIVORS AND NON SURVIVORS

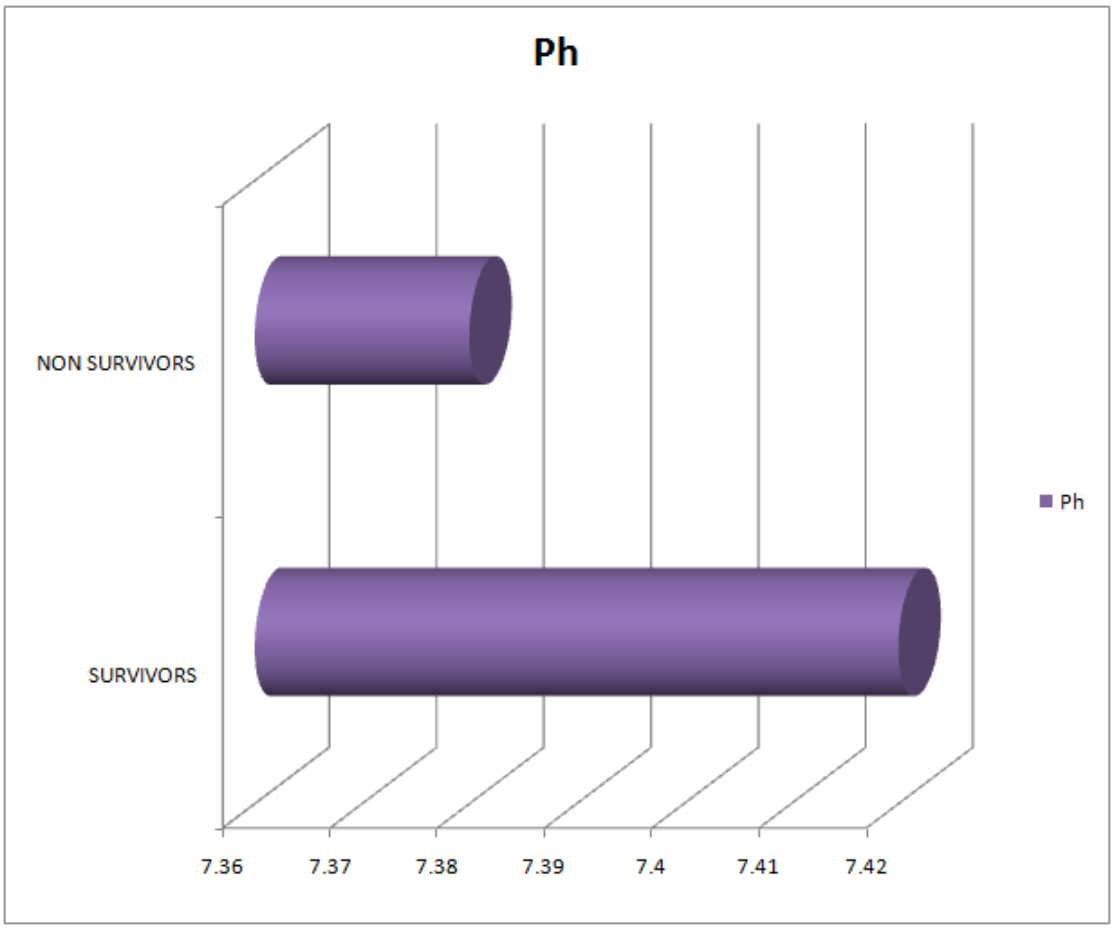


pH AND ITS CORRELATION WITH MORTALITY

PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
pH	7.42	0.1	7.38	0.1	1.4	*0.08*

The pH of blood does not show any direct relationship with survival as evidenced by a p value of more than 0.05.

BAR DIAGRAM SHOWING THE AVERAGE VALUES OF pH IN SURVIVORS AND NON SURVIVORS

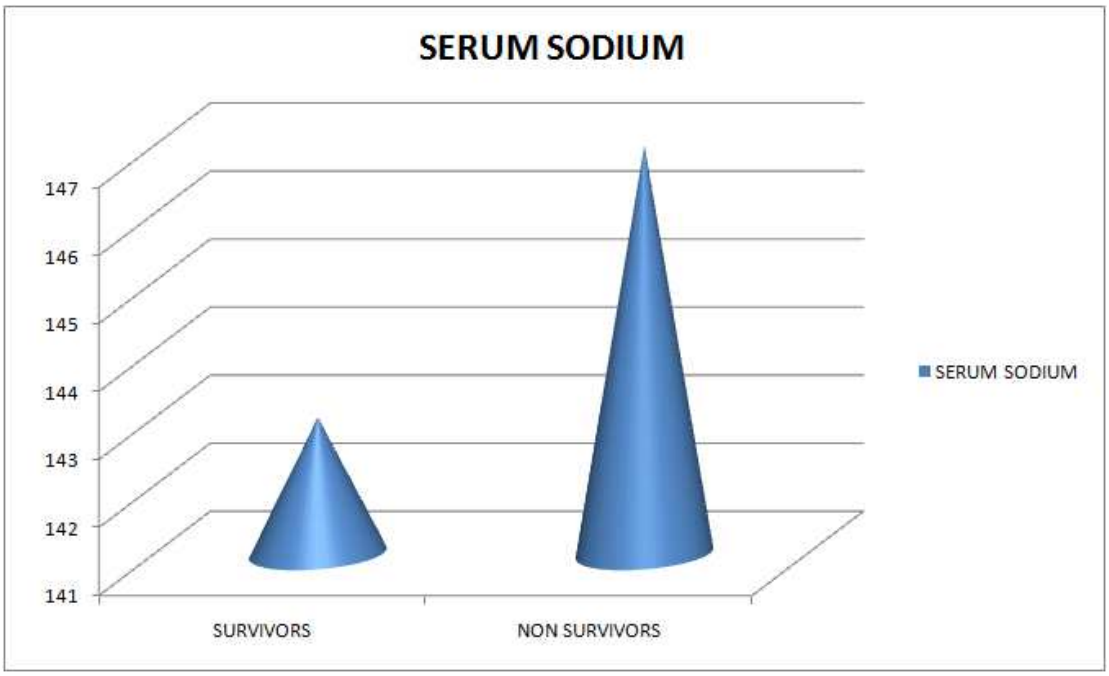


SERUM SODIUM AND ITS CORRELATION WITH MORTALITY

PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
SERUM SODIUM	142	9.73	146.9	7.4	1.97	*0.02*

Serum sodium, thus has an average value of 142 in survivors and 146 in non survivors. Since the p value is less than 0.05 , this indicates a significant correlation.

BAR DIAGRAM SHOWING THE MEAN SERUM SODIUM VALUES IN SURVIVORS AND NON SURVIVORS

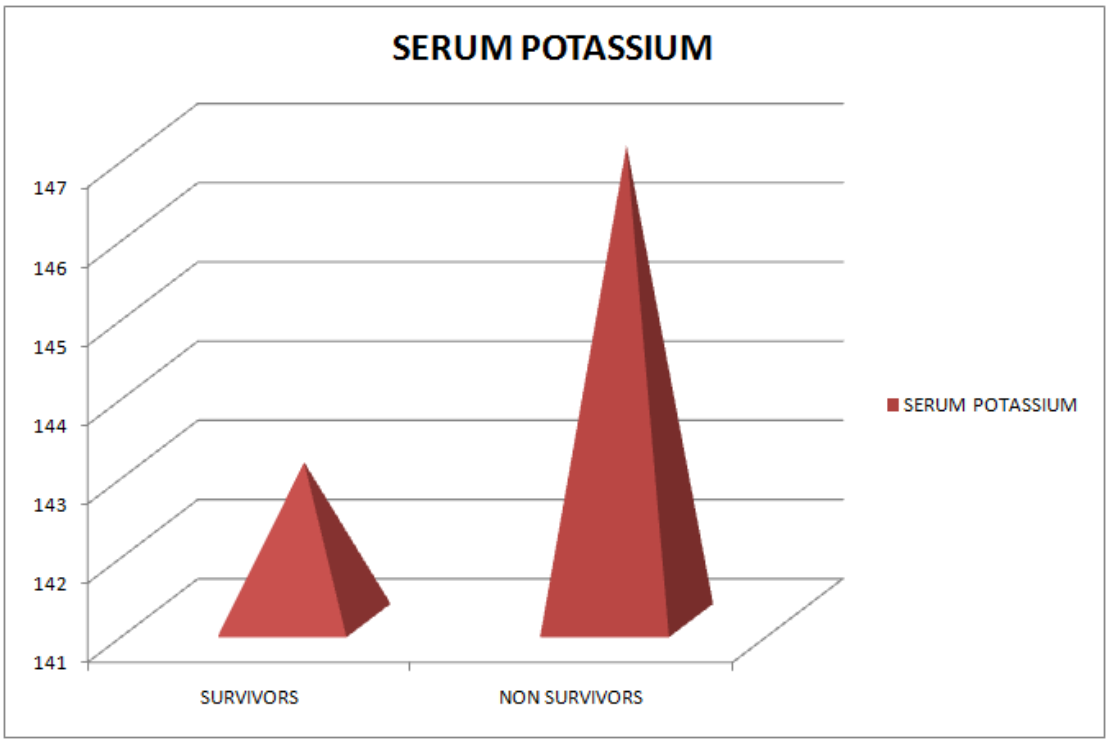


SERUM POTASSIUM AND ITS CORRELATION WITH MORTALITY

PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
SERUM POTASSIUM	3.92	0.9	3.63	1.6	0.87	*0.19*

The serum potassium value does not correlate with mortality in patients with Sepsis – MODS.

BAR DIAGRAM SHOWING THE CORRELATION BETWEEN SERUM POTASSIUM AND MORTALITY



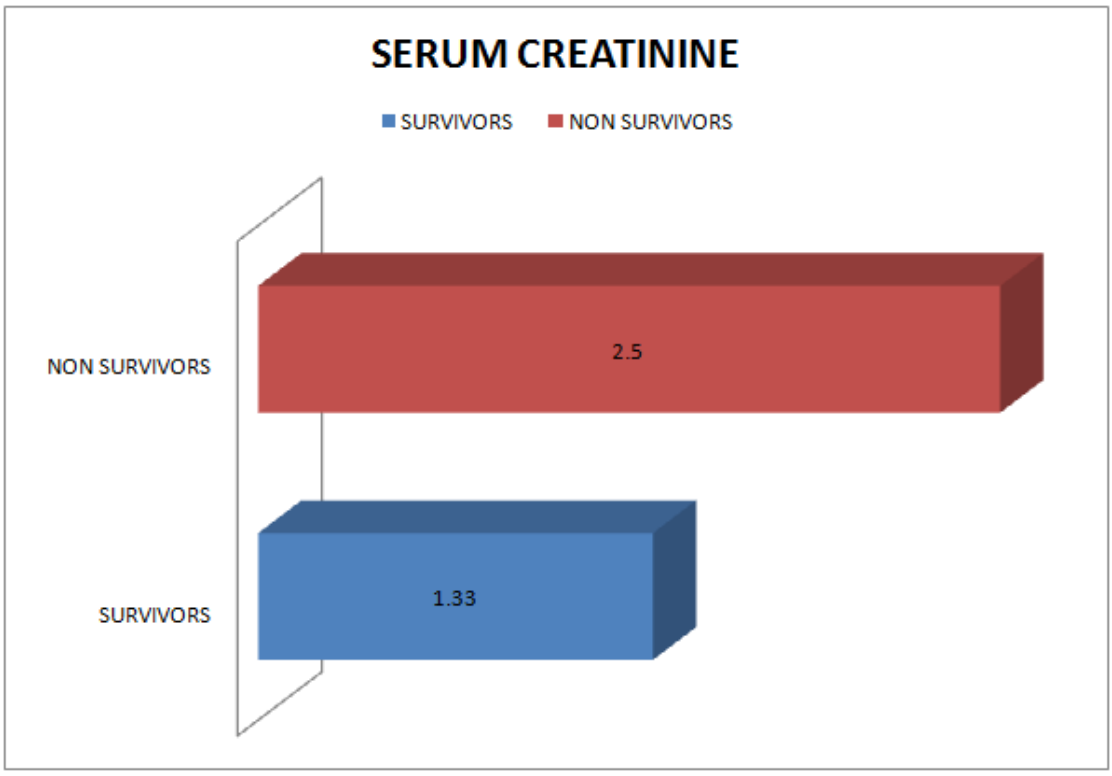
SERUM CREATININE AND ITS CORRELATION WITH MORTALITY

PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
SERUM CREATININE	1.33	0.62	2.5	1.21	4.84	*P < 0.05*

Since the p value is less than 0.05 , there is a definite correlation between increased creatinine and mortality risk in patients with Sepsis – MODS.

The average value of creatinine is found to be higher in non survivors than non survivors (2.5 Vs 1.33)

BAR DIAGRAM SHOWING THE CORRELATION BETWEEN SERUM CREATININE AND MORTALITY

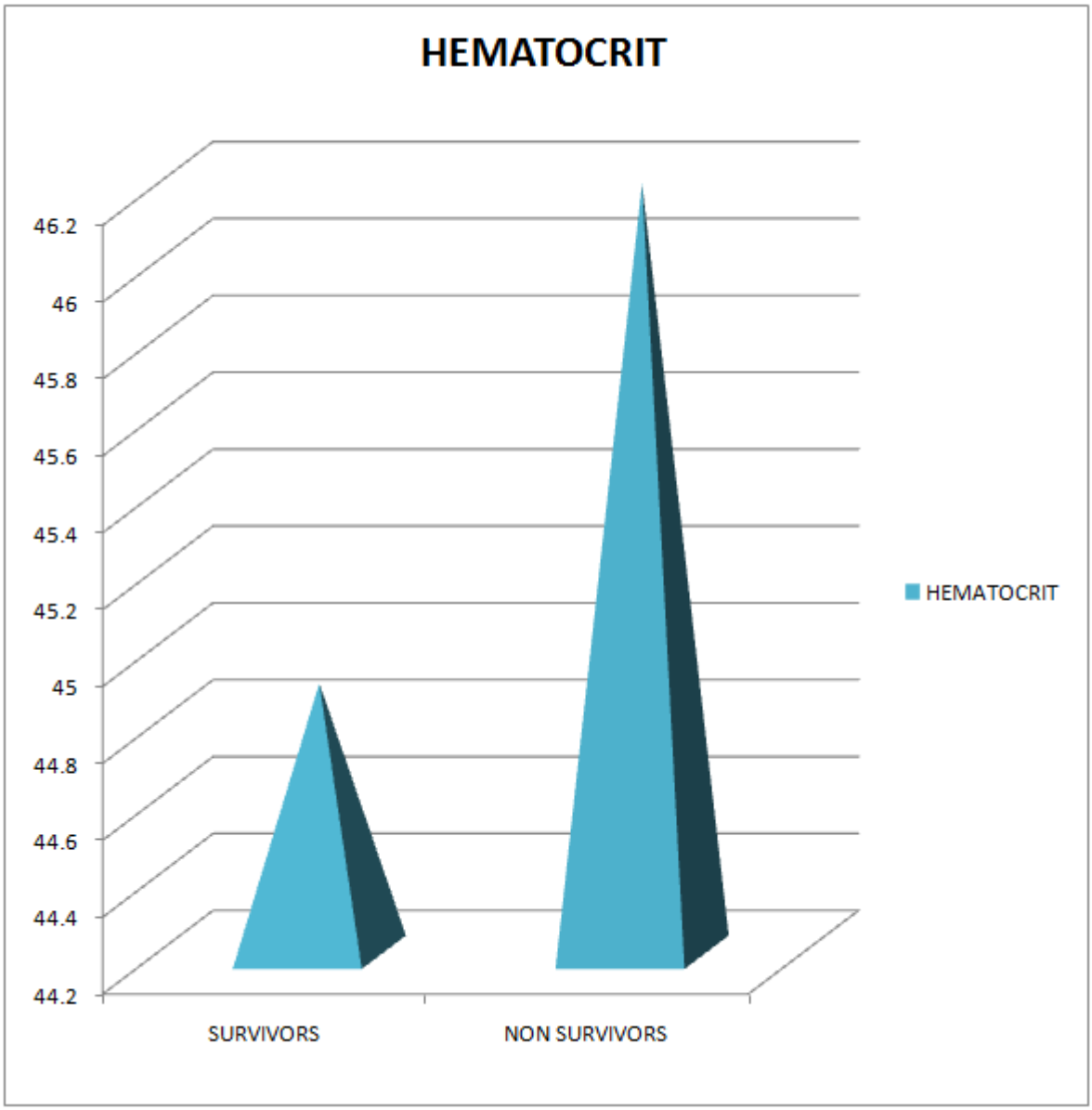


HEMATOCRIT AND ITS CORRELATION WITH MORTALITY

PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
HEMATOCRIT	44.9	7.14	46.2	6.8	0.69	*0.24*

Hematocrit does not exhibit any definitive correlation with mortality in our study (p = 0.24)

BAR DIAGRAM SHOWING THE AVERAGE HEMATOCRIT VALUES IN SURVIVORS AND NON SURVIVORS

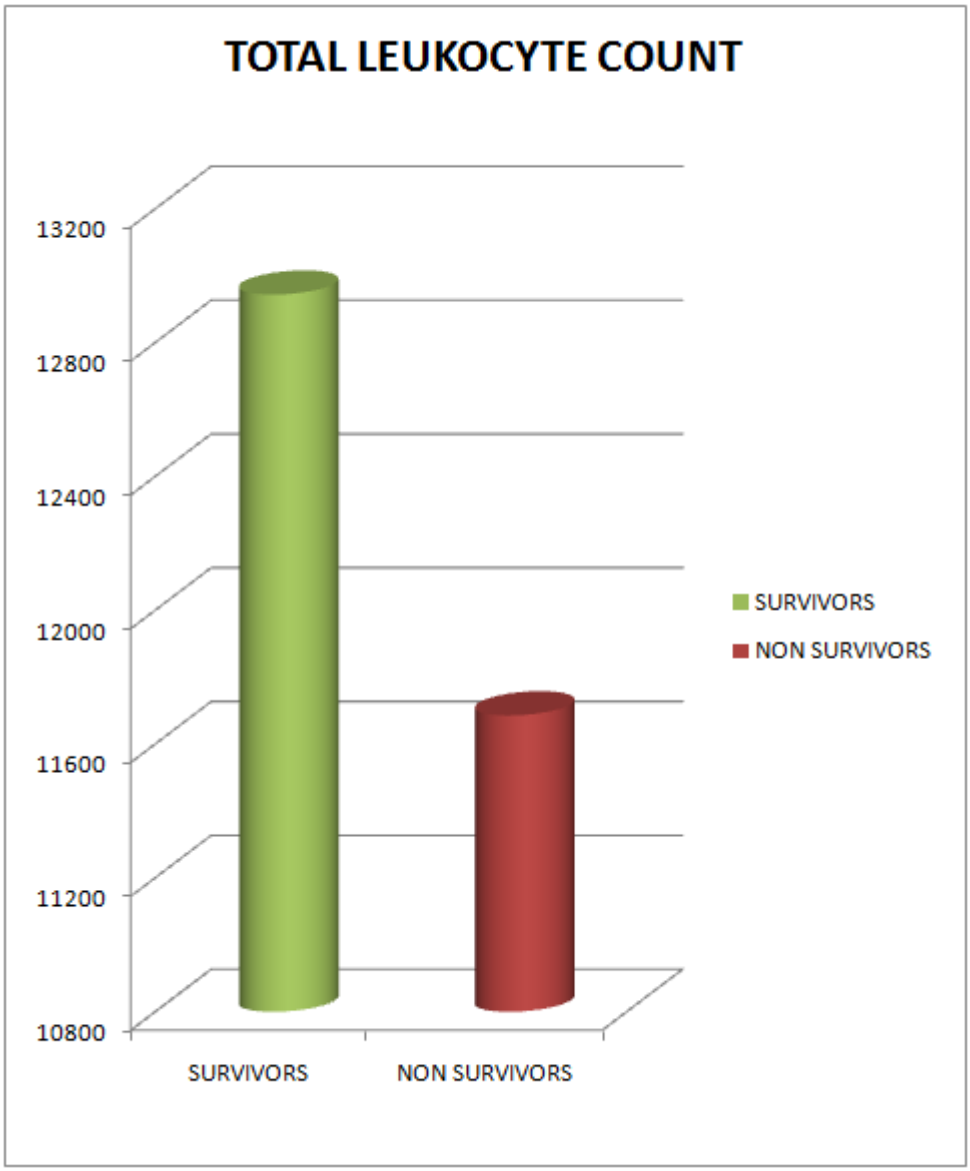


TOTAL LEUKOCYTE COUNT AND ITS CORRELATION WITH MORTALITY

PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
TOTAL LEUKOCYTE COUNT	12,944	5977	11,686	4909	0.82	*0.20*

The total leukocyte count does not appear to have independent direct correlation with mortality in patients with Sepsis – MODS.

BAR DIAGRAM SHOWING THE MEAN LEUKOCYTE COUNTS IN SURVIVORS AND NON SURVIVORS



GLASGOW COMA SCALE AND ITS CORRELATION WITH MORTALITY

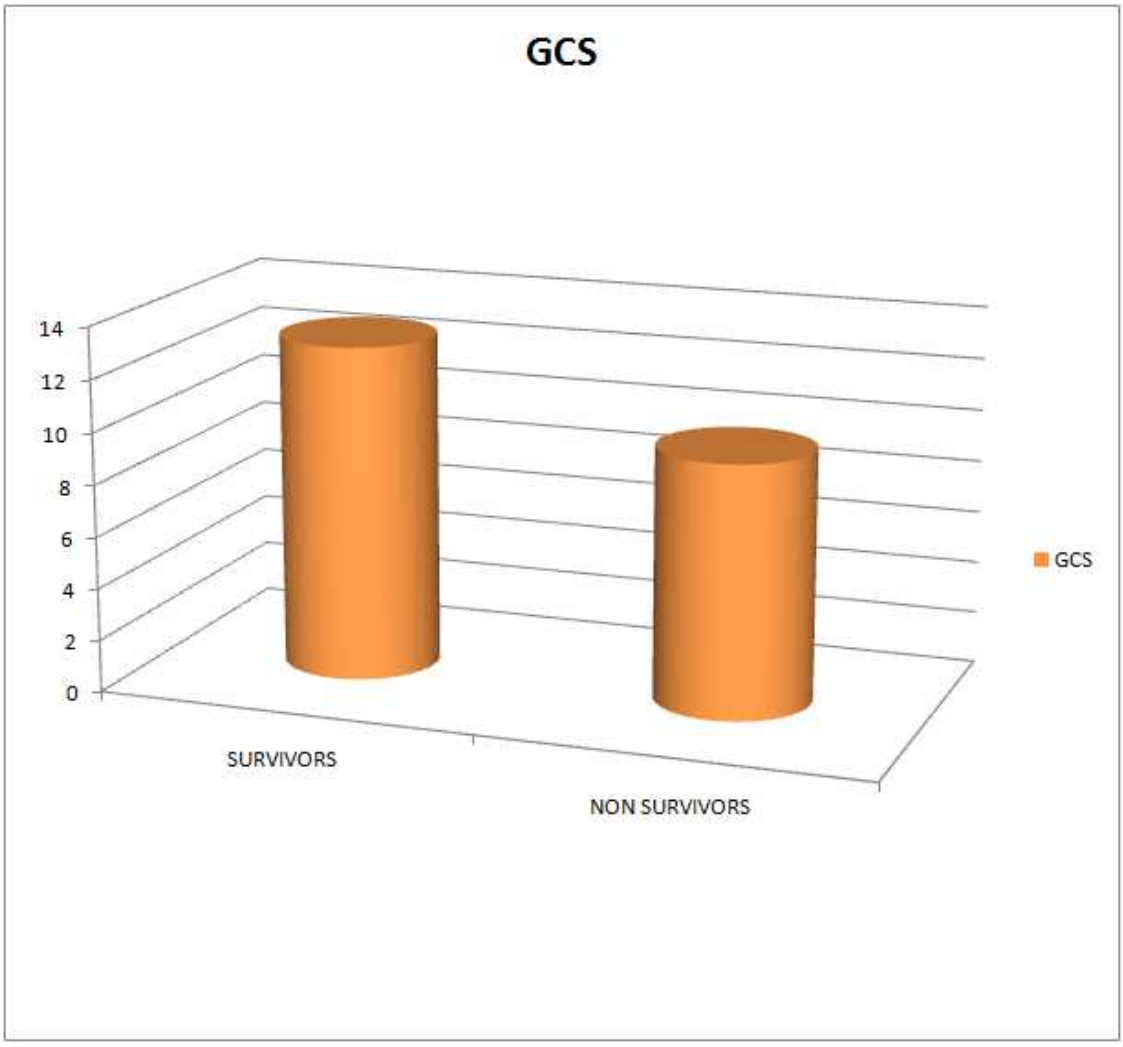
PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
GLASGOW COMA SCALE	12.9	2	9.7	2.3	5.6	*< 0.05*

Glasgow coma scale has an independent correlation with mortality in sepsis – MODS in our study.

A lower GCS appears to be associated with a higher mortality risk

The mean GCS in survivors was 13 while that in non survivors was much lower at 9

BAR DIAGRAM SHOWING THE AVERAGE GLAGOW COMA SCALE IN SURVIVORS AND NON SURVIVORS



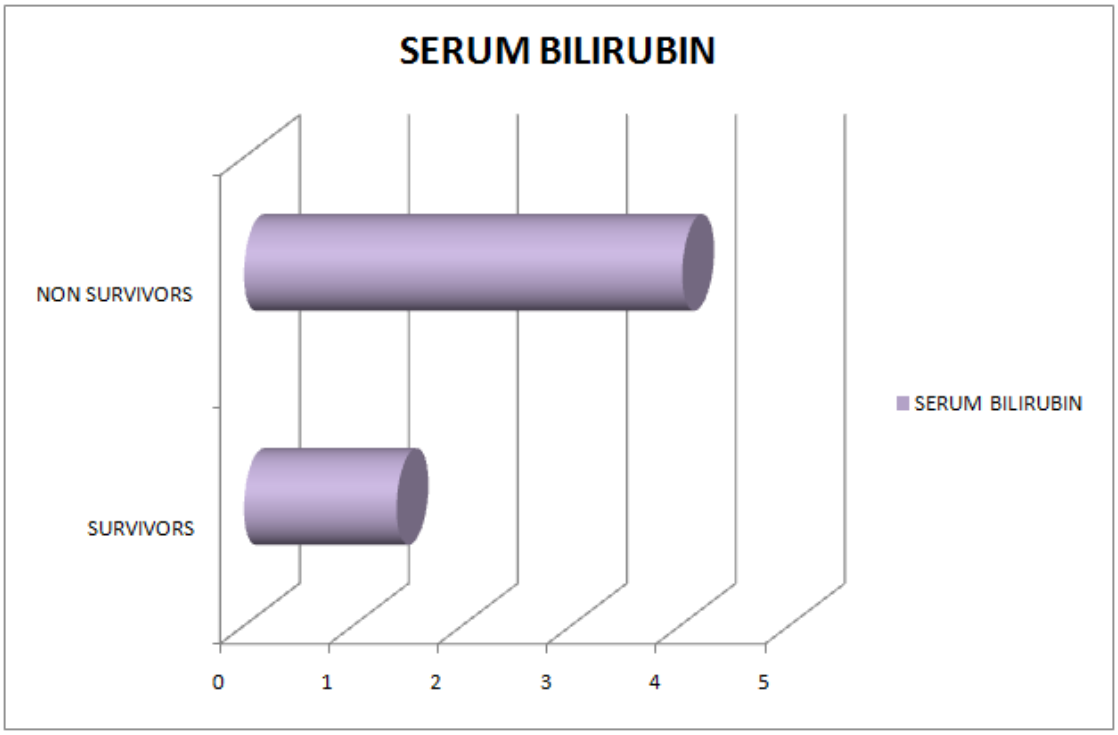
SERUM BILIRUBIN AND ITS CORRELATION WITH MORTALITY

PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
SERUM BILIRUBIN	1.4	0.54	4.02	3.3	4.64	*< 0.05*

Serum bilirubin , which is one of the variables taken into account in the calculation of the SOFA score is found to have a positive correlation with mortality in our study.

The mean total bilirubin was higher in the mortality group than among the survivors (4 Versus 1.4)

BAR DIAGRAM SHOWING THE AVERAGE SERUM BILIRUBIN IN SURVIVORS AND NON SURVIVORS

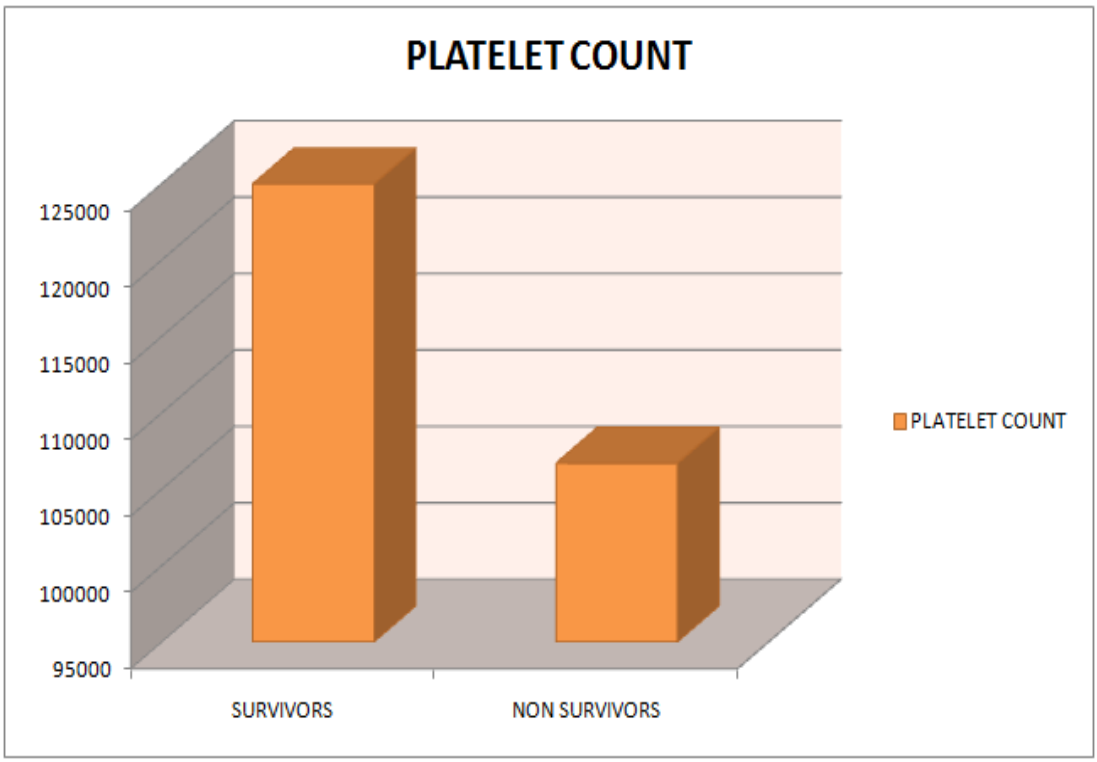


PLATELET COUNT AND ITS CORRELATION WITH MORTALITY

PARAMETER	SURVIVORS		NON SURVIVORS		T SCORE	P VALUE
	MEAN	STANDARD DEVIATION	MEAN	STANDARD DEVIATION		
PLATELET COUNT	124973	67000	106700	49900	1.09	*0.13*

The platelet count does not exhibit any definitive correlation with mortality in our study (p = 0.13)

BAR DIAGRAM SHOWING THE AVERAGE PLATELET COUNTS IN SURVIVORS AND NON SURVIVORS



DISCUSSION

DISCUSSION

This study was conducted as a prospective and retrospective observational study in patients admitted with Sepsis – Multi organ Dysfunction Syndrome in the intensive medical care wards of Madras Medical College and Rajiv Gandhi Government General Hospital. The sample size was 60. After getting the informed consent of the patients and their attending close relatives , the patients were subjected to history taking, physical examination and relevant laboratory testing and imaging. These were done to ascertain the presence of sepsis and multi organ dysfunction in the patient.

Sepsis – Multi organ dysfunction syndrome is a major cause of mortality in India and worldwide. Hence a better understanding of its etiopathogenesis and the disease course is necessary. Further, the application of prognostication tools like the APACHE II score and the SOFA score aid in assessing the prognosis and help the care givers in making improved decisions.

APACHE II score has shown good correlation with several critical care states, including Sepsis – multi organ dysfunction syndrome. Several studies have been conducted to compare its effectiveness against the other

newly developed scoring systems like SOFA and the SAPS score. Some studies have supported APACHE II while others concluded that SOFA was better.

A study by Q Qiao et al comparing the APACHE 2 and SOFA score in critically ill elderly patients showed that SOFA had a better predictive capacity of mortality than APACHE 2[90].

Another study by K.S. Abinandan et al also showed that serial SOFA was a better mortality indicator in cases of sepsis and MODS[91].

However studies by K.M. Ho, K.Y. Lee et al showed that APACHE II score was a better predictor of mortality than SOFA score[92]

In our study both the scores were compared with each other and their component variables were also evaluated as individual predictors of mortality.

The APACHE II score was shown to have good correlation with mortality in cases of Sepsis – Multi organ Dysfunction syndrome. A higher APACHE II score was associated with mortality.

The SOFA scores (SOFA I , SOFA III and mean SOFA) were all noted to have good predictive correlation with mortality. These scores were noted to be higher in the non survivor group. All three showed a p

value of less than 0.05. However the lowest absolute value of p was noted in SOFA III. Also, in the survivor group the day 1 SOFA score was low and it further reduced on day 3. But among the non survivors the day 1 SOFA score itself was higher and this increased further on day 3. This indicates that probably a daily monitoring of the SOFA score is more important than a single value and that progressively increasing score is more predictive of mortality than absolute values.

Apart from these scores, some of their component variables namely the heart rate, respiratory rate, serum sodium, serum creatinine, Glasgow coma scale and serum bilirubin were also noted to have significant ($p < 0.05$) correlation with mortality in sepsis – MODS.

However pAO2 , pH , hematocrit , platelet count and total WBC count did not show any correlation with mortality.

CONCLUSION

CONCLUSION

Both the APACHE II score and SOFA scores (SOFA I , SOFA III and the mean SOFA scores) were noted to have significant correlation with 30 day mortality in cases of sepsis – multi organ dysfunction syndrome.

Higher values of APACHE 2, SOFA 1 , SOFA 3 scores were associated with higher mortality

A serial monitoring of SOFA scores on consecutive days is a better prognostication tool than a single value. A rising SOFA score on subsequent days is likely to be associated with higher mortality risk.

Heart rate, respiratory rate , serum sodium, serum creatinine , Glasgow coma scale and serum bilirubin were also noted to have independent correlation with mortality in these patients.

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LIMITATIONS

LIMITATIONS OF THE STUDY

A multi centric study with a larger sample size and longer follow up is essential to assess the predictive power of these prognostication tools in a more comprehensive manner.

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BIBLIOGRAPHY

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ANNEXURES

COMPARATIVE ANALYSIS OF APACHE-II SCORE AND SOFA SCORE AS PREDICTORS OF MORTALITY IN PATIENTS ADMITTED WITH SEPSIS AND MODS

PROFORMA

Name :
Age/Sex :
Address :
Occupation :
IP number :
Date of Admission :
Date of Discharge / Death :

SYMPTOMS:

Fever
Altered sensorium
Respiratory distress
Jaundice
Bleeding manifestations
Reduced urine output
Cold clammy extremities

PAST HISTORY :

DM	
SHT	
CKD	
CAD	
COPD	
DCLD	

GENERAL EXAMINATION:

GCS	

VITAL SIGNS:

PR -
BP -
MAP -
RR -
TEMP -
URINE OUTPUT -

SYSTEMIC EXAMINATION :

CVS:

RS:

ABDOMEN:

CNS:

INVESTIGATIONS:

COMPLETE HEMOGRAM

RENAL FUNCTION TESTS

SERUM ELECROLYTES

SERUM BILIRUBIN

ARTERIAL BLOOD GAS ANALYSIS

BLOOD CULTURE

URINE CULTURE

FEVER PROFILE

ASSESSMENT OF APACHE II AND THE SOFA SCORES

AGE	SEX	CO MORBIDS	DURATION OF STAY	APACHE II SCORE	SOFA SCORE			30 DAY SURVIVAL YES/NO
					SOFA I	SOFA III	MEAN SOFA	

ETHICAL COMMITTEE APPROVAL

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No. 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr.E.Senthilkumar
Postgradaute M.D.(General Medicine)
Madras Medical College
Chennai 600 003

Dear Dr.E.Senthilkumar,

The Institutional Ethics Committee has considered your request and approved your study titled **"Comparative analysis of APACHE2 and SOFA scores in patients admitted with sepsis and multi organ dysfunction syndrome in RGGGH" No.05052015.**

The following members of Ethics Committee were present in the meeting held on 12.05.2015 conducted at Madras Medical College, Chennai-3.

1.	Prof.C.Rajendran, M.D.,	: Chairperson
2	Prof.R Vimala, M.D., Dean, MMC, Ch-3	: Deputy Chairperson
3.	Prof.B.Kalaiselvi, M.D., Vice-Principal, MMC, Ch-3	: Member Secretary
4.	Prof.B.Vasanthi, M.D., Prof. of Pharmacology, MMC	: Member
5.	Prof.P Ragumani, M.S., Professor of Surgery, MMC	: Member
6.	Prof.Saraswathy, M.D., Director, Pathology, MMC, Ch-3	: Member
7.	Prof.K.Srinivasagalu, M.D.,Director, I.I.M. MMC, Ch-3	: Member
8.	Thiru S Rameshkumar, B.Com., MBA	: Lay Person
9.	Thiru S.Govindasamy, B.A., B.L.,	: Lawyer
10.	Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

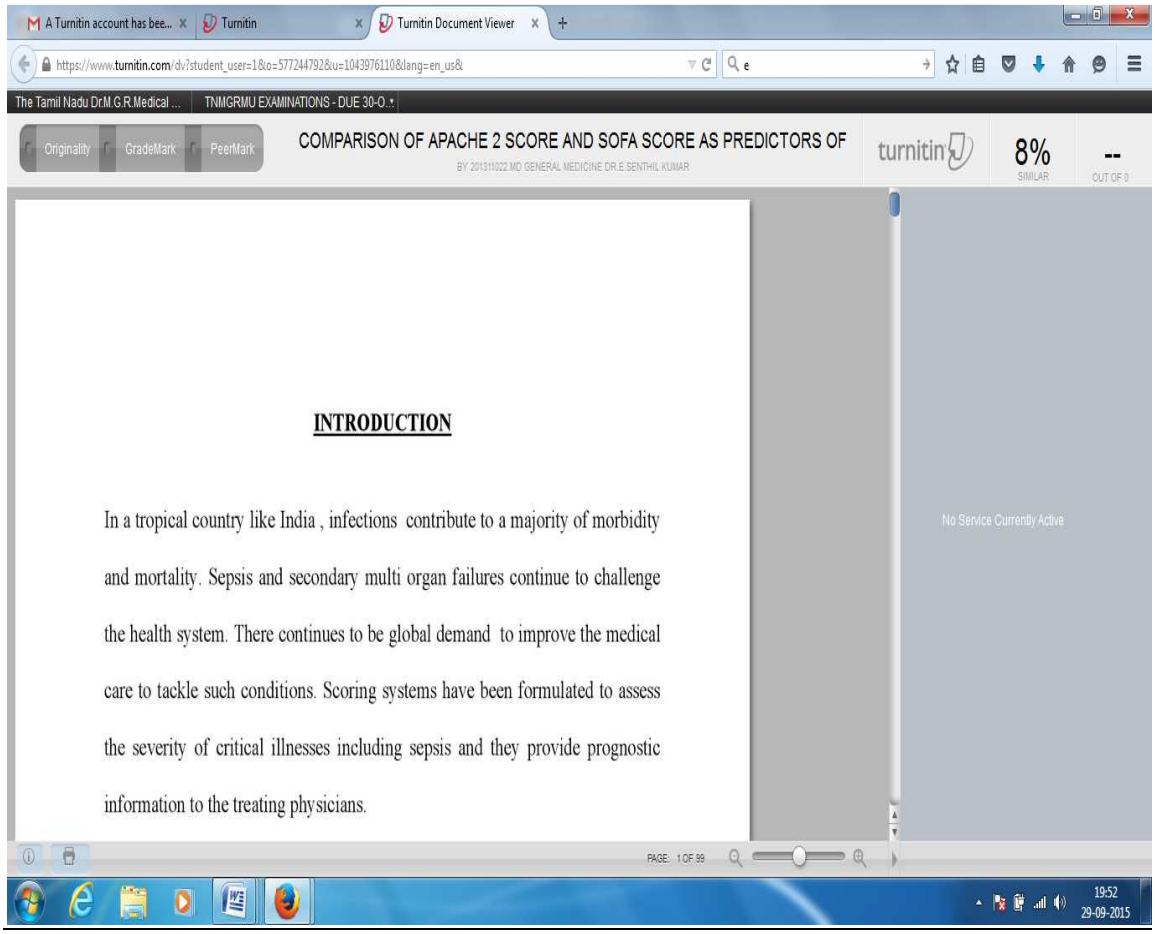
We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

15/6/15

Member Secretary, Ethics Committee
MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLE

PLAGIARISM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INTRODUCTION
In a tropical country like India , infections contribute to a majority of morbidity and mortality. Sepsis and secondary multi organ failures continue to challenge the health system. There continues to be global demand to improve the medical care to tackle such conditions. Scoring systems have been formulated to assess the severity of critical illnesses including sepsis and they provide prognostic information to the treating physicians.
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INFORMATION SHEET

We are conducting a study on **"COMPARATIVE ANALYSIS OF APACHE-II SCORE AND SOFA SCORE AS PREDICTORS OF MORTALITY IN PATIENTS ADMITTED WITH SEPSIS AND MULTI ORGAN DYSFUNCTION SYNDROME "** among patients admitted in intensive care medical wards in Rajiv Gandhi Government General Hospital, Chennai and for that your specimen may be valuable to us.

The purpose of this study is to assess the risk stratification using the APACHE 2 and SOFA scores of patients admitted with sepsis and MODS.

We are selecting certain cases and if you are found eligible, we may be using your blood samples to do certain tests which in any way do not affect your final report or management.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator Signature of Participant/attending relative

Date :

Place :

ஆராய்ச்சி தகவல் தாள்

சென்னை ராஜீவ்காந்தி அரசு பொது மருத்துவமனையின் பொது மருத்துவத்துறையில் "அப்பாச்சி-2 மற்றும் சோஃபா அளவீடுகளை குறுகி நஞ்சு-பல்லுறுப்பு செயல் பிறழ்ச்சியின் இறப்பு விகிதத்தின் குறிகாட்டிகளாய் ஒப்பிட்டு ஆராய்தல்" பற்றிய ஆய்வு நடைபெறுகிறது.

நீங்களும் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம். இதனால் தங்களது சிகிச்சையில் பாதிப்பு ஏற்படாது என்பதையும் தெரிவித்துக்கொள்கிறோம்.

இந்த ஆய்வில் தங்களுக்கு மருத்துவபரிசோதனை, இரத்தப் பரிசோதனை, ஸ்கேன், சிறுநீர் பரிசோதனை மற்றும் எக்ஸ்ரே (X-Ray) பரிசோதனை செய்யப்படும்.

முடிவுகளை அல்லது கருத்துக்களை வெளியிடும்போதோ அல்லது ஆராய்ச்சியின்போதோ தங்களது பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டோம் என்பதை தெரிவித்துக்கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய விருப்பத்தின்பேரில்தான் இருக்கிறது. மேலும் நீங்கள் எந்த நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

இந்த சிறப்பு பரிசோதனைகளின் முடிவுகளையும் நோயின் தன்மை பற்றியும் ஆராய்ச்சியின்போது அல்லது ஆராய்ச்சியின் முடிவின்போது தங்களுக்கு அறிவிப்போம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

பங்கேற்பாளர் கையொப்பம்

ஆராய்ச்சியாளர் கையொப்பம்

நாள் :
இடம் :

PATIENT CONSENT FORM

Study Detail : **" COMPARATIVE ANALYSIS OF APACHE-II SCORE AND SOFA SCORE AS PREDICTORS OF MORTALITY IN PATIENTS ADMITTED WITH SEPSIS AND MODS "**

Study Centre : Rajiv Gandhi Government General Hospital, Chennai.

Patient's Name :

Patient's Age :

Identification Number

Patient may check (√) these boxes

a) I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ❑

b) I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected . ❑

c) I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ❑

d) I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms. ❑

e) I hereby consent to participate in this study.

f) I hereby give permission to undergo detailed clinical examination and blood investigations as required. ❑

Signature / thumb impression of pt / attending relative

Patient's Name and Address

Signature of Investigator

Study Investigator's Name:

Dr. SENTHIL KUMAR .E .

சுய ஒப்புதல் படிவம்

ஆராய்ச்சி தலைப்பு :

அப்பாச்சி 2 மற்றும் சோபா அளவீடுகளை, குறுதி நஞ்சு - பல்லுறுப்பு செயல் பிறழ்ச்சி நோயின் குறிகாட்டிகளாக ஒப்பிட்டு ஆராய்தல்

பெயர்	வயது
பால்	தேதி
உள் நோயாளி எண்	ஆராய்ச்சி சேர்க்கை எண்

இந்த ஆராய்ச்சியின் விவரங்களும் நோக்கங்களும் எனக்கு முழுமையாகவும் தெளிவாகவும் விளக்கப்பட்டன. எனக்கு விளக்கப் பட்ட விஷயங்களை நான் புரிந்து கொண்டு எனது சம்மதத்தை தெரிவிக்கிறேன்.

மேற்கொண்ட பரிசோதனையின் பொழுது ஏற்படக்கூடிய பின் விளைவுகளை உணர்ந்து இந்த பரிசோதனைக்கு மனமாற சம்மதிக்கிறேன்.

இந்த ஆய்வுக்கான பரிசோதனைகளை செய்து கொள்ள சம்மதிக்கிறேன். இந்த ஆராய்ச்சியின் விளக்க தாளை பெற்றுக்கொண்டேன். இந்த ஆய்வில் முழு சுதந்திரத்துடன் மற்றும் சுய நினைவுடன் பங்கு கொள்ள சம்மதிக்கிறேன்.

பங்கேற்ப்பாளர் / பாதுகாவலர் கையொப்பம்

தேதி

MASTER CHART

S.No	SEX	AGE	CHR HEALTH	TEMP	MAP	HR	RR	PaO2	pH	SODIUM	POTASSIUM	CREATININE	HCT	TC	GCS	APACHE II	SURVIVAL
1	M	49	2	37.2	114	120	18	86	7.3	135	3.7	0.5	47	16000	12	17	YES
2	F	55	2	37.6	86	116	16	70	7.2	137	3.9	0.6	48	18000	11	18	YES
3	M	32	2	38	112	112	20	85	7.5	151	4.4	1.1	45	21000	10	16	YES
4	F	46	2	38.6	126	144	52	79	7.32	151	5.6	1.9	34	15300	13	24	NO
5	M	44	2	38.6	56	110	26	66	7.35	142	4.3	1.6	52	17000	10	20	YES
6	F	65	2	38.5	62	64	25	70	7.33	136	4	1.2	47	2800	8	33	YES
7	M	80	2	38	120	124	32	66	7.36	149	1.5	1.8	57	16000	9	32	NO
8	M	70	2	38.7	108	130	13	90	7.24	152	2.7	1.8	53	15000	11	26	YES
9	F	57	2	39	60	80	27	70	7.5	158	2.8	3.2	58	16000	14	23	YES
10	M	34	2	38.6	54	100	32	74	7.33	128	3.9	1.7	48	8000	13	17	YES
11	M	20	2	38.6	108	70	32	52	7.48	148	2.7	1.3	47	2700	11	16	NO
12	F	55	2	37.8	50	138	34	50	7.5	145	2.5	3.4	51	17000	14	26	NO
13	F	65	2	38.8	100	122	26	73	7.47	154	2.6	1.4	44	3500	6	26	YES
14	F	39	2	38.6	110	112	12	70	7.51	132	3.7	1	47	12600	14	12	YES
15	F	57	2	41	57	122	25	58	7.5	130	5.9	1.9	45	17200	10	28	NO
16	M	55	2	38.2	114	102	28	60	7.58	142	4.9	0.8	37	15600	15	12	YES
17	F	64	2	37	112	134	32	60	7.31	157	2.5	1.8	58	14900	9	30	NO
18	M	42	2	38.8	54	52	20	71	7.42	151	2.8	1.8	45	18000	15	15	YES
19	F	27	2	38.6	120	138	34	84	7.48	136	2.8	1	48	15000	15	13	YES
20	F	40	2	36.4	62	162	44	84	7.32	147	1.6	5.8	44	7000	11	22	NO

S.No	SEX	AGE	CHR HEALTH	TEMP	MAP	HR	RR	PaO2	pH	SODIUM	POTASSIUM	CREATININE	HCT	TC	GCS	APACHE II	SURVIVAL
21	M	50	2	38.6	86	90	32	80	7.56	154	4.9	0.8	47	5000	12	12	YES
22	M	79	2	38	102	100	16	78	7.35	149	3.6	1.3	48	18000	12	14	YES
23	M	51	2	38.2	110	137	48	75	7.28	150	2.9	3.5	32	3000	10	25	NO
24	F	83	2	38.2	72	100	32	76	7.45	149	3.7	1.9	58	21000	12	19	YES
25	F	48	2	36.6	116	104	26	74	7.33	150	3.2	1	36	8000	14	12	YES
26	F	79	2	38.8	NR	162	30	58	7.3	148	6	4.9	47	15000	8	36	NO
27	M	51	2	38.6	112	96	27	66	7.58	152	3.7	0.9	47	15700	14	14	YES
28	M	26	2	37	78	102	20	70	7.25	147	5.4	3.2	46	3800	10	19	NO
29	F	53	2	38.6	65	57	31	88	7.49	150	2.8	0.7	34	8000	15	15	YES
30	M	70	2	38.8	60	64	10	30	7.3	147	3.9	1.1	46	17300	13	17	YES
31	M	72	2	38.6	54	129	32	56	7.37	145	3.3	1.7	47	15900	7	32	NO
32	F	64	2	37	50	110	36	84	7.25	156	5.1	3.4	42	13000	9	27	NO
33	M	69	2	39	130	106	20	76	7.35	128	5.1	0.9	34	9000	13	17	YES
34	F	70	2	38.5	110	112	28	66	7.52	136	4.7	1.5	56	16000	15	13	YES
35	M	36	2	38	100	142	25	66	7.58	144	1.9	3.3	50	5600	13	18	NO
36	F	34	2	38.2	122	113	30	63	7.35	149	2.9	2.9	37	7900	8	21	NO
37	M	44	2	37.6	96	119	24	69	7.33	147	5.5	1.5	39	11000	12	17	NO
38	M	40	2	38	66	98	40	55	7.25	130	3.6	1.8	46	3000	15	14	YES
39	M	55	2	37	120	113	15	65	7.5	120	5.6	1.5	36	14900	15	14	YES
40	M	40	2	38.6	78	112	26	64	7.34	151	4.5	0.9	48	24900	14	11	YES

S.No	SEX	AGE	CHR HEALTH	TEMP	MAP	HR	RR	PaO2	pH	SODIUM	POTASSIUM	CREATININE	HCT	TC	GCS	APACHE II	SURVIVAL
41	F	77	2	38	NR	154	33	60	7.35	144	3.1	2.7	47	18000	4	37	NO
42	F	46	2	38	126	108	26	69	7.48	149	2.6	0.6	29	2700	13	17	YES
43	F	69	2	38.6	64	127	27	54	7.29	138	1.5	1.5	49	9800	10	29	NO
44	F	72	2	39	52	110	28	62	7.34	135	5.6	1.9	42	22000	14	22	YES
45	F	46	2	38	109	108	42	94	7.57	155	5.4	2.7	40	11000	11	24	NO
46	M	69	2	38.4	110	117	13	64	7.58	132	3.6	1.4	33	15000	13	16	YES
47	F	30	2	36.8	108	109	19	70	7.5	156	4	1.4	46	15000	12	15	YES
48	M	22	2	37	140	72	34	70	7.49	132	5.3	1.7	48	17000	10	23	NO
49	M	61	2	37.8	106	135	26	61	7.39	144	2.6	1.3	49	14800	13	17	YES
50	F	70	2	38.6	72	54	30	60	7.49	124	3.1	1.3	38	8000	12	19	YES
51	F	42	2	38	112	129	36	66	7.52	137	4.9	1.8	49	7500	11	20	NO
52	F	37	2	37.8	108	117	11	80	7.5	150	3.2	3.4	49	15500	12	20	YES
53	M	40	2	38.4	90	68	14	86	7.4	136	3.9	1	46	14900	13	12	YES
54	M	55	2	37	54	104	26	60	7.45	136	4.2	0.8	32	15600	15	12	YES
55	F	60	2	36.4	56	138	16	66	7.49	148	4.3	2.1	47	1500	15	19	YES
56	M	55	2	37.8	64	112	27	60	7.39	156	2.7	0.3	52	15700	6	31	NO
57	M	62	2	39	64	119	15	70	7.28	130	5.5	0.6	49	13600	15	17	YES
58	F	59	2	38.6	72	124	26	76	7.28	158	1.7	2.1	57	12800	7	27	NO
59	M	40	2	38	120	128	26	54	7.52	150	5.6	1.5	38	11000	14	16	YES
60	M	31	2	38.8	100	122	34	60	7.34	140	5	1.4	55	3000	13	17	YES

S.No	AGE	SEX	PaO2/FiO2		BILIRUBIN		PLATELET COUNT		MAP		CREATININE		GCS		SOFA				
			DAY 1	DAY 3	DAY 1	DAY 3	DAY 1	DAY 3	DAY 1	DAY 3	DAY 1	DAY 3	DAY 1	DAY 3	DAY 1	30 DAY SURVIVAL	DAY 3	30 DAY SURVIVAL	MEAN SOFA
1	49	M	320	330	1	1.1	133000	166000	114	110	0.5	0.6	12	14	6	YES	4	YES	5
2	55	F	345	330	1.3	1	122000	137000	86	90	0.6	0.7	11	12	6	YES	5	YES	5.5
3	32	M	306	312	1.1	1.2	114000	166000	112	110	1.1	1.2	10	11	6	YES	5	YES	5.5
4	46	F	302	230	7.1	13	24000	18000	126	80	1.9	2	13	12	9	NO	12	NO	10.5
5	44	M	290	295	0.7	1.1	141000	133000	56	66	1.6	1.7	10	10	9	YES	9	YES	9
6	65	F	194	198	1.5	1.3	90000	95000	62	70	1.2	1.1	8	9	11	YES	11	YES	11
7	80	M	321	300	13.1	15	36000	25000	120	80	1.8	2.4	9	8	12	NO	14	NO	13
8	70	M	196	237	2.3	1.1	131000	149000	108	110	1.8	2.5	11	12	9	YES	10	YES	9.5
9	57	F	231	279	2.1	2	164000	155000	60	80	3.2	1.1	14	14	7	YES	8	YES	7.5
10	34	M	321	347	1.1	1.2	115000	210000	54	70	1.7	1.5	13	14	7	YES	6	YES	6.5
11	20	M	150	270	1.5	3.8	57000	64000	108	84	1.3	1.9	11	10	9	NO	11	NO	10
12	55	F	84	92	3.1	4.5	17100	164000	50	56	3.4	3.2	14	13	10	NO	10	NO	10
13	65	F	360	342	2	3	164000	170000	100	102	1.4	2.1	8	10	7	YES	7	YES	7
14	39	F	352	330	0.7	1.2	122000	145000	110	108	1	1.1	14	14	4	YES	4	YES	4
15	57	F	250	267	1.8	2.7	45000	37000	57	72	1.9	2	10	11	10	NO	12	NO	11
16	55	M	307	310	0.5	0.9	113000	136000	114	108	0.8	0.9	15	15	3	YES	3	YES	3
17	64	F	107	112	5.7	8.4	61000	49000	112	106	1.8	1.8	9	8	11	NO	13	NO	12
18	42	M	299	294	1.1	1.1	177000	203000	54	66	1.8	1.9	15	14	5	YES	5	YES	5
19	27	F	312	304	1	1.2	92000	123000	120	110	1	0.9	15	15	5	YES	4	YES	4.5
20	40	F	205	231	2	4.3	92000	78000	62	75	5.8	5.1	11	10	13	NO	14	NO	13.5

S.No	AGE	SEX	PaO2/FiO2		BILIRUBIN		PLATELET COUNT		MAP		CREATININE		GCS		SOFA				
			DAY 1	DAY 3	DAY 1	DAY 3	DAY 1	DAY 3	DAY 1	DAY 3	DAY 1	DAY 3	DAY 1	DAY 3	DAY 1	30 DAY SURVIVAL	DAY 3	30 DAY SURVIVAL	MEAN SOFA
21	50	M	300	345	0.9	1	127000	136000	86	90	0.8	1.1	12	12	5	YES	5	YES	5
22	79	M	290	298	1.3	1.8	211000	223000	102	108	1.3	1.4	12	13	6	YES	5	YES	5.5
23	51	M	377	297	1.9	3.4	377000	204000	110	98	3.5	4.2	10	8	9	NO	12	NO	10.5
24	83	F	374	352	1.2	1.2	314000	312000	72	90	1.9	1.1	12	12	6	YES	5	YES	5.5
25	48	F	351	366	1.5	1.4	78000	90000	116	110	1	1.1	14	15	6	YES	6	YES	6
26	79	F	76	84	8.4	10	111000	108000	NR	NR	4.9	5	8	8	15	NO	15	NO	15
27	51	M	299	298	1.3	1.4	144000	149000	112	104	0.9	1	14	15	5	YES	5	YES	5
28	26	M	210	NA	1	NA	70000	NA	78	NA	3.2	NA	10	NA	9	NO	NA	NO	NA
29	53	F	272	266	1.5	1.4	161000	201000	65	84	0.7	1.1	15	15	4	YES	4	YES	4
30	70	M	303	312	2.1	1.9	92000	96000	60	72	1.1	0.9	13	14	7	YES	6	YES	6.5
31	72	M	90	176	5.5	6	82000	78000	54	60	1.7	1.9	7	7	11	NO	11	NO	11
32	64	F	292	150	3.2	5	131000	98000	50	NR	3.4	5	9	10	11	NO	13	NO	12
33	69	M	311	400	1.1	1.1	127000	92000	130	128	0.9	1.4	13	12	7	YES	7	YES	7
34	70	F	342	345	1.8	1.4	97000	99000	110	110	1.2	1.2	15	15	3	YES	3	YES	3
35	36	M	188	98	0.8	1.4	22000	34000	100	98	3.3	3.5	13	12	10	NO	12	NO	11
36	34	F	132	230	1.3	1.2	72000	90000	122	118	2.9	2.7	8	9	11	NO	10	NO	10.5
37	44	M	300	NA	1.9	NA	87000	NA	96	NA	1.5	NA	12	NA	7	NO	NA	NO	NA
38	40	M	354	366	3	2.2	96000	90000	66	90	1.8	1.6	15	15	5	YES	4	YES	4.5
39	55	M	372	380	1	0.9	118000	123000	120	126	1.5	1.1	15	15	4	YES	3	YES	3.5
40	40	M	298	316	0.7	0.8	121000	134000	78	92	0.9	1	14	15	4	YES	3	YES	3.5

S.No	AGE	SEX	PaO2/FiO2		BILIRUBIN		PLATELET COUNT		MAP		CREATININE		GCS		SOFA				
			DAY 1	DAY 3	DAY 1	DAY 3	DAY 1	DAY 3	DAY 1	DAY 3	DAY 1	DAY 3	DAY 1	DAY 3	DAY 1	30 DAY SURVIVAL	DAY 3	30 DAY SURVIVAL	MEAN SOFA
41	77	F	180	174	11	13	112000	98000	NR	NR	2.7	2.6	4	5	14	NO	15	NO	14.5
42	46	F	342	378	1.2	1.1	147000	149000	126	112	0.6	0.7	13	14	4	YES	4	YES	4
43	69	F	75	84	7	9	97000	62000	64	60	1.5	2.5	10	11	13	NO	14	NO	13.5
44	72	F	331	366	1.9	1.2	86000	112000	52	70	1.9	1.5	14	14	7	YES	5	YES	6
45	46	F	204	198	3	7	81000	89000	109	110	2.7	3	11	11	11	NO	13	NO	12
46	69	M	352	370	2	2.1	119000	137000	110	106	1.4	1.5	13	14	6	YES	6	YES	6
47	30	F	307	315	1.9	2	139000	146000	108	105	1.4	1.3	12	14	6	YES	5	YES	5.5
48	22	M	204	210	4	4.5	176000	144000	140	132	1.7	1.8	10	11	10	NO	10	NO	10
49	61	M	318	366	2.1	1.9	261000	278000	106	105	1.3	1.4	13	14	5	YES	5	YES	5
50	70	F	304	421	1.5	1.4	78000	89000	72	86	1.3	1.4	12	12	6	YES	5	YES	5.5
51	42	F	104	NA	2.2	NA	181000	NA	112	NA	1.8	NA	11	NA	8	NO	NA	NO	NA
52	37	F	293	312	2.2	1.1	94000	99000	108	102	3.4	3	12	12	9	YES	9	YES	9
53	40	M	307	292	1	1.1	108000	144000	90	96	1	1.1	13	14	3	YES	4	YES	3.5
54	55	M	370	388	1	0.8	117000	146000	54	66	0.8	0.9	15	15	3	YES	3	YES	3
55	60	F	362	379	1.9	1.8	34000	48000	56	64	2.1	1.9	15	15	7	YES	6	YES	6.5
56	55	M	70	NA	1.1	NA	104000	NA	64	NA	0.3	NA	6	NA	11	NO	NA	NO	NA
57	62	M	318	345	1.1	1.7	143000	147000	64	70	0.6	0.9	15	15	3	YES	4	YES	3.5
58	59	F	270	240	1.9	2	147000	144000	72	70	2.1	2.4	7	8	NA	NO	12	NO	11.5
59	40	M	355	404	1.2	1.2	76000	88000	120	110	1.5	1.3	14	14	6	YES	5	YES	5.5
60	31	M	313	392	0.9	1	149000	144000	100	106	1.4	1.5	13	12	9	YES	9	YES	9

KEY TO MASTER CHART

APACHE	acute physiology and chronic health evaluation score
SOFA	serial organ failure assessment
TEMP	temperature in degrees celsius
HR	heart rate
PaO2	partial pressure of oxygen in mm Hg
FiO2	fractional inspired oxygen
HCT	hematocrit
GCS	Glasgow coma scale